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# **ReFReSH**

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*Restriction For Reorganising Sleep Habit:*

*A randomised controlled trial of simplified sleep restriction for  
primary insomnia in the primary care setting*

**Dr Karen Frances Falloon**

**A thesis submitted in fulfilment of the requirements for the degree of  
Doctor of Philosophy in General Practice,  
The University of Auckland, 2014**

## Abstract

**Rationale:** Insomnia is a common health problem for patients in primary care. A literature review conducted by the author concluded that cognitive behavioural therapy for insomnia (CBT-I) is effective but its use has been limited by the time and expense required for delivery. Sleep restriction, or restricting the time in bed, is one component of CBT-I, which could be delivered as a brief intervention during primary care consultations. A systematic review of sleep restriction as a stand-alone treatment for insomnia showed some benefit, but concluded that more evidence was required.

**Objective:** To assess the effectiveness of simplified sleep restriction to improve sleep in primary insomnia.

**Design, Setting, and Participants:** A randomised controlled trial involving adult patients with persistent primary insomnia recruited from general practice clinics in Auckland, New Zealand between 2009 and 2012.

**Intervention:** Intervention patients received 20 minutes of sleep hygiene advice and “simplified sleep restriction” instructions at an initial visit with a general practitioner and 14 minutes of advice and a “sleep self-adjustment algorithm” at two weeks. Control patients received sleep hygiene advice alone at both visits.

**Main outcomes:** The primary outcomes were change in sleep quality at six months as measured by the Pittsburgh Sleep Quality Index (PSQI), the Insomnia Severity Index (ISI), and sleep efficiency. Proportion reaching a pre-defined “treatment response” was calculated using PSQI and sleep efficiency. Secondary outcomes included sleepiness, fatigue, sleep-onset latency, wakefulness after sleep onset, total sleep time, depression and anxiety. Potential adverse events (excessive sleepiness, accidents, hospitalisations, physiological parameters) were monitored.

**Results:** Ninety-seven patients were recruited and 94 (97%) completed the study. Simplified sleep restriction led to significantly improved PSQI scores (6.2 vs 8.4,  $p < 0.001$ ), ISI scores (8.6 vs 11.1,  $p = 0.001$ ); sleep efficiency (difference between mean changes 2.2%,  $p = 0.006$ ) and sleep onset latency (difference between mean changes -6.1 minutes,  $p = 0.04$ ) as measured by actigraphy; and a reduction in fatigue (difference between mean changes -2.3 units,  $p = 0.04$ ) compared with control. Simplified sleep restriction also produced higher rates of “treatment response” (67% [28/42] vs 41% [20/49]), with an adjusted odds ratio of 2.7 (95% CI, 1.1 to 6.5;  $p = 0.03$ ). There were no significant differences in other outcomes or adverse effects.

**Conclusions and Relevance:** Simplified sleep restriction is a practical, effective intervention for chronic insomnia in adults suitable for the primary care setting.

To my husband Matt. Thank you.

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## List of Abbreviations

|           |   |
|-----------|---|
| ADHB      | Auckland District Health Board  |
| ACTH      | Adrenocorticotrophic hormone  |
| BBTI      | Brief Behavioural Treatment for Insomnia  |
| BMI       | Body mass index   |
| BP        | Blood pressure  |
| CAGE      | Questionnaire for detecting alcohol dependency  |
| CBT-I     | Cognitive behavioural therapy for insomnia  |
| CONSORT   | Consolidated Standards of Reporting Trials  |
| CRF       | Corticotrophin-releasing factor   |
| DBP       | Diastolic blood pressure  |
| DSM-IV    | Diagnostic and Statistical Manual of Mental Disorders, Fourth edition                 |
| DSM-IV-TR | Diagnostic and Statistical Manual of Mental Disorders, Fourth edition – text revision |
| ESS       | Epworth Sleepiness Scale  |
| FFS       | Flinders Fatigue Scale  |
| GABA      | Gamma amino-butyric acid  |
| GAD-7     | Generalised Anxiety Disorder 7-item assessment  |
| GLM       | General linear model  |
| GP        | General Practitioner  |
| HPA       | Hypothalamic-pituitary axis   |
| HR        | Heart rate  |
| ICSD-2    | International Classification of Sleep Disorders, Second edition                       |

|            |  |
|------------|--|
| ISI        | Insomnia Severity Index                  |
| MLST       | Multiple sleep latency test              |
| MMRM       | Mixed model repeated measures            |
| NREM       | Non-rapid eye movement                   |
| OSA        | Obstructive sleep apnoea                 |
| PHQ-9      | Patient Health Questionnaire             |
| PLMS       | Periodic limb movements of sleep         |
| PROC MIXED | The mixed linear model procedure         |
| PSG        | Polysomnography                          |
| PSQI       | Pittsburgh Sleep Quality Index           |
| RDC        | Research diagnostic criteria             |
| ReFReSH    | Restriction for Reorganising Sleep Habit |
| RLS        | Restless legs syndrome                   |
| SBP        | Systolic blood pressure                  |
| SE         | Sleep efficiency                         |
| SOL        | Sleep onset latency                      |
| SSR        | Simplified sleep restriction             |
| SSRI       | Selective serotonin reuptake inhibitors  |
| SWA        | Slow wave activity                       |
| SWS        | Slow wave sleep                          |
| TIA        | Transient ischaemic attack               |
| TIB        | Time in bed                              |

TST Total sleep time

WASO Wake after sleep onset



# Chapter 1 Introduction

## 1.1 Background

Insomnia is a sleep disorder characterised by difficulty initiating sleep, maintaining sleep, or sleep that is “non-restorative” or poor in quality (American Psychiatric Association, 2000; American Sleep Disorders Association, 2005). A diagnosis of an insomnia disorder requires daytime symptoms of impairment or distress that are related to the difficulty with sleeping (American Psychiatric Association, 2000; American Sleep Disorders Association, 2005). Examples of daytime impairments include: fatigue, problems with concentration or memory, mood disturbance or irritability, proneness to errors, reduced motivation, headaches, gastrointestinal symptoms, and worries about sleep (American Sleep Disorders Association, 2005). In addition, these symptoms must occur despite the individual having adequate time and opportunity for sleep. This latter condition helps to distinguish insomnia from sleep deprivation (American Sleep Disorders Association, 2005).

The symptom of insomnia affects approximately 40% of adults in the general population with between 7% and 22% meeting the criteria for an insomnia disorder (Leger, Poursain, Neubauer, & Uchiyama, 2008; Ohayon & Reynolds, 2009; T. Roth et al., 2011). The prevalence of insomnia in the primary care setting is even higher with approximately 40% of patients meeting criteria for an insomnia disorder (Bruce Arroll et al., 2012; Leger, Guilleminault, Dreyfus, Delahaye, & Paillard, 2000). As well as being highly prevalent, insomnia tends to have a persistent and recurrent nature (Buysse et al., 2008; Morin, Belanger, et al., 2009; Morphy, Dunn, Lewis, Boardman, & Croft, 2007). Chronic insomnia is also associated with a number of negative health consequences, such as an increased risk of depression and anxiety (Baglioni et al., 2011; Ford & Kamerow, 1989), cardiovascular disease (Laugsand, Vatten, Platou, & Janszky, 2011; Sofi et al., 2012; Suka, Yoshida, & Sugimori, 2003; Vgontzas, Liao, Bixler, Chrousos, & A., 2009), and lower quality of life (Leger et al., 2012).

In the primary care setting, approximately 12% of those with insomnia suffer from primary insomnia (Bruce Arroll et al., 2012). Primary insomnia refers to insomnia that is not better explained by, or does not occur exclusively during the course of another medical or psychiatric condition (for example, depression or anxiety), substance abuse, or another sleep disorder (for example, obstructive sleep apnoea or restless legs syndrome) (American Psychiatric Association, 2000). Put into context, for a general practitioner who consults patients for 30 hours per week this equates to approximately six patients per week meeting the diagnostic criteria for primary insomnia. Many of these patients will go undiagnosed and untreated despite the negative medical, social, and professional consequences of

chronic insomnia (Leger, Guilleminault, Bader, Levy, & Paillard, 2002; Siriwardena et al., 2009; Sivertsen, Nordhus, Bjorvatn, & Pallesen, 2009).

## **1.2 Why Treat Insomnia?**

### **1.2.1 Insomnia as a persistent condition**

Insomnia is often a persistent or recurring condition. Longitudinal studies have reported approximately 40 to 50 per cent of those with insomnia at baseline also have insomnia at follow up of 2 to 20 years duration (Breslau, Roth, Rosenthal, & Andreski, 1996; Buysse et al., 2008; Ganguli, Reynolds, & Gilby, 1996; Hohagen et al., 1993; Kim et al., 2009; Livingston, Blizard, & Mann, 1993; Mallon, Broman, & Hetta, 2000). Randomised controlled trials of insomnia treatment demonstrate that improvements in sleep quality and quality of life can be achieved by many of those with insomnia (Buysse et al., 2011; Edinger & Sampson, 2003; Espie et al., 2007; Krystal, 2007; Morin, Colecchi, Stone, Sood, & Brink, 1999; Morin, Vallieres, et al., 2009; Walsh et al., 2007).

### **1.2.2 Insomnia has a negative impact on health, wellbeing, and functioning**

A growing body of literature suggests that insomnia has a negative impact on health and wellbeing as well as causing difficulties with social, intellectual, and vocational functioning (Fortier-Brochu, Beaulieu-Bonneau, Ivers, & Morin, 2012; Kucharczyk, Morgan, & Hall, 2012; Leger & Bayon, 2010; Léger, Guilleminault, Bader, Lévy, & Paillard, 2002; Matteson-Rusby, Pigeon, Gehrman, & Perlis, 2010; Taylor, Lichstein, & Durrence, 2003). The evidence for the association with impaired mental health, particularly depression and anxiety, cardiovascular disease, development of the metabolic syndrome, and the impact upon quality of life and social and vocational functioning is presented below.

#### **Mental health**

Insomnia and depression often occur together (Baglioni et al., 2011; Buysse et al., 2008). Insomnia is now considered to be a “comorbid” condition when it occurs in those with depression, rather than being a condition “secondary” to depression (Baglioni et al., 2011). There is a large amount of evidence in the literature to suggest that insomnia is also a risk factor for the development of depression (both new-onset and recurrent depression) (Breslau et al., 1996; Buysse et al., 2008; Chang, Ford, Mead, Cooper-Patrick, & Klag, 1997; Cho et al., 2008; Foley, Monjan, Simonsick, Wallace, & Blazer, 1999; Ford & Kamerow, 1989; Jansson-Frojmark & Lindblom, 2008; Kim et al., 2009; Livingston et al., 1993; Mallon et al., 2000; Morphy et al., 2007; Perlis et al., 2006; R. E. Roberts, Shema, Kaplan, & Strawbridge, 2000; Szklo-Coxe, Young, Peppard, Finn, & Benca, 2010; Vollrath, Wicki, & Angst, 1989; Weissman, Greenwald, Murcia, & Dement, 1997). A meta-analytic evaluation of longitudinal studies investigating both insomnia and depression symptoms showed that non-depressed people with insomnia had a twofold risk of developing depression compared to people with no sleep difficulties

(odds ratio 2.10,  $p < 0.001$ , 95% CI [1.86, 2.38]) (Baglioni et al., 2011). The results were also similar when both a working age group and an elderly group were analysed separately (Baglioni et al., 2011). In those with depression, poor sleep contributes to depression severity and is associated with poor response to depression treatment (Pigeon et al., 2008). Residual insomnia after depression treatment is also a risk factor for subsequent depression relapse (Dombrovski et al., 2008; Dombrovski et al., 2007; Reynolds et al., 1997). A review of prospective studies found those with insomnia were up to six times more likely to develop anxiety disorders than those without insomnia (Taylor et al., 2003). Suicide may also be associated with insomnia (Pigeon, 2010). One study in adolescent suicide completers showed those completing suicide were five times more likely to have insomnia in the week before death than age-matched controls even after controlling for depressive symptoms (Goldstein, Bridge, & Brent, 2008). Those with insomnia, or a history of insomnia, have also been shown to be at higher risk for developing an anxiety disorder than those without a history of insomnia (Breslau et al., 1996; Ford & Kamerow, 1989). A cross-sectional study in a community-based sample of adults ( $n = 772$ ) showed people with insomnia were 17 times more likely to experience clinically significant anxiety than those without insomnia demonstrating the close relationship between the two conditions ( $p < 0.001$ , 95% CI [7.6, 39.5]) (Taylor, Lichstein, Durrence, Reidel, & Bush, 2005). A history of insomnia is also a risk factor for the development of alcohol abuse or dependence disorders (Breslau et al., 1996; Ford & Kamerow, 1989; Weissman et al., 1997), as well as being a risk factor for relapse in alcoholism (Brower, Aldrich, Robinson, Zucker, & Greden, 2001; Drummond, Gillin, Smith, & DeModena, 1998).

### **Cardiovascular disease**

Insomnia is associated with an increased risk of both hypertension and coronary heart disease (Laugsand et al., 2011; Suka et al., 2003; Vgontzas et al., 2009). A recent meta-analysis of prospective cohort studies investigating insomnia and cardiovascular disease showed that insomnia conferred a 45% increased risk of developing or dying from cardiovascular disease during follow up (relative risk 1.45,  $p < 0.001$ , 95% CI [1.3, 1.6]) (Sofi et al., 2012).

In addition, Vgontzas et al. (2009) conducted a cross-sectional investigation looking at the association between insomnia and hypertension. They found that compared to normal sleepers, and those with a sleep duration greater than six hours, those with a short sleep duration had an increased risk of hypertension (<5 hours sleep: odds ratio 5.1, 95% CI [2.2, 11.8]; 5-6 hours sleep odds ratio 3.5, 95% CI [1.6, 7.9];  $p < 0.01$ ) (Vgontzas et al., 2009). Suka et al. (2003) conducted a prospective cohort study examining the association between persistent difficulty initiating sleep or maintaining sleep with the development of hypertension in middle-aged Japanese male workers. After adjusting for potential confounding factors they found that both insomnia complaints were significantly associated with the development of hypertension (difficulty initiating sleep odds ratio 2.0, 95% CI [1.4, 2.7] and difficulty

maintaining sleep odds ratio 1.9, 95% CI [1.5, 2.5]) (Suka et al., 2003). Laugsand et al. (2011) conducted a large prospective study investigating insomnia as a risk factor for coronary heart disease. Participants in a large Norwegian health survey ( $n = 52,610$ ) were asked questions relating to insomnia at baseline as well as having cardiovascular risk factors assessed (for example, blood pressure and fasting cholesterol). They were then followed for 11 years or to first acute myocardial infarction (heart attack). After adjusting for established cardiovascular risk, depression, and anxiety; a history of insomnia was associated with a moderately increased risk of myocardial infarction (difficulty initiating sleep 1.5, 95% CI [1.2, 1.8] and difficulty maintaining sleep 1.3, 95% CI [1.0, 1.7]) (Laugsand et al., 2011). It is important to note that an association between insomnia and myocardial infarction does not necessarily imply that insomnia causes myocardial infarction. However, the prospective evidence does support a directional link.

### **Metabolic syndrome**

The metabolic syndrome (hyperglycaemia, central adiposity, hypertension, hypertriglyceridaemia, and low high density lipoprotein cholesterol) is a key risk factor for cardiovascular disease (Lakka et al., 2002). There is growing evidence that sleep symptoms are associated with the development of the metabolic syndrome. A recently reported study by Troxel et al. (2010) reported that specific symptoms of insomnia (difficulty falling asleep and “unrefreshing” sleep) were significant predictors for the development of the metabolic syndrome. A diagnosis of insomnia meeting diagnostic criteria consisting of at least one insomnia-related sleep complaint, occurring at least twice a week, and at least one symptom of daytime impairment was not a significant predictor of the metabolic syndrome, but did show a trend towards this association (Troxel et al., 2010). Previous research has also shown an association between difficulty falling asleep and the incidence of diabetes (Nilsson, Roost, Engstrom, Hedblad, & Berglund, 2004).

### **Quality of life, social and vocational functioning**

Those with chronic insomnia experience significantly impaired quality of life compared to good sleepers and as insomnia worsens, quality of life deteriorates (Leger, Scheuermaier, Philip, Paillard, & Guilleminault, 2001; Zammit, Weiner, Damato, Sillup, & McMillan, 1999). A large cross-sectional survey spanning three continents also showed that those with chronic primary insomnia have significantly lower quality of life scores compared to good sleepers (Leger et al., 2012). This study by Leger et al. (2012) suggested the impact of chronic primary insomnia on quality of life scores was comparable to that seen in chronic illnesses such as diabetes and depression. In primary care patients, chronic insomnia has been associated with a decreased ability to enjoy family and social life, a decreased ability to handle minor irritations, a poorer relationship with spouse, and lower rating of health and quality of life compared to good sleepers (Shochat, Umphress, Israel, & Ancoli-Israel,

1999). In a well-defined population with chronic primary insomnia, significant impairments in vitality, social functioning, and mental health have been demonstrated compared with US normative reference values (Walsh et al., 2007).

Those with primary insomnia have also been shown to score significantly worse than good sleepers in prospectively measured daytime symptoms of alertness, positive and negative mood, and sleepiness/fatigue (Buysse et al., 2007). A meta-analysis of the effects of primary insomnia on cognitive function has also demonstrated significant impairments in those with primary insomnia compared to good sleepers in episodic memory, problem solving, working memory (retention and manipulation), reaction time, information processing, and selective attention (Fortier-Brochu et al., 2012).

Primary insomnia has also shown a significant association with the risk of non-workplace injuries (as well as workplace injuries) (Kessler et al., 2012). Reduced sleep duration (less than five hours) and sleepiness have also been associated with an increased risk of serious motor vehicle accidents (Connor et al., 2002).

In the vocational domain, insomnia has been associated with significantly reduced work performance, absenteeism, and increased risk of work-place injury (Daley, Morin, LeBlanc, Gregoire, & Savard, 2009; Godet-Cayre et al., 2006; Kessler et al., 2011). The estimated costs related to this loss in productivity and the increased health care costs are substantial for individuals, employers, and society. Studies conducted in France, the United States, and Canada estimate this cost per person annually to be approximately \$2700, \$3000, and \$6500 (NZD<sup>1</sup>), respectively (Godet-Cayre et al., 2006; Kessler et al., 2011).

### **1.3 Why Is Insomnia Not Adequately Treated?**

Studies estimate that approximately 40 to 60 per cent of those with chronic insomnia have not discussed their insomnia with a doctor (Aikens & Rouse, 2005; Morin, LeBlanc, Daley, Gregoire, & Merette, 2006; Sarsour, Kalsekar, Swindle, Foley, & Walsh, 2011; Shochat et al., 1999). For those that have sought help for their insomnia, the general practitioner (GP) is consulted more frequently than any other health professional (Morin, LeBlanc, et al., 2006; Stinson, Tang, & Harvey, 2006). As well as those with chronic insomnia having low help-seeking behaviour, the literature also suggests that insomnia is inadequately treated in primary care (Siriwardena et al., 2009; Sivertsen et al., 2009). As a consequence, many of those who suffer from chronic insomnia who seek help from their general

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<sup>1</sup> Conversion to New Zealand Dollar (NZD) conducted retrospectively based on the date of submission of each article.

practitioner receive pharmacological treatment for insomnia despite evidence that non-pharmacological treatment has equivalent short term benefits and superior long term benefits (Siriwardena et al., 2009). In a study from the United Kingdom linking a postal survey about insomnia with primary care records it was found that despite primary care consultation, two-thirds of the insomnia sample had persistent insomnia symptoms at 12 month follow up (Hayward, Jordan, & Croft, 2012). This suggests both that insomnia is persistent, but that it also may be inadequately or ineffectively treated. This is further supported by a survey of general practitioners from the United States regarding sleep knowledge and attitudes which suggested that the majority of general practitioners have a low rate of expertise and comfort relating to the management of sleep disorders (Papp, Penrod, & Strohl, 2002). A survey of general practitioners' treatment of insomnia in Norway reported that sleep hygiene advice was the most common treatment for insomnia, followed by zopiclone (a hypnotic), and then non-pharmacological treatments (Sivertsen et al., 2009). In addition, hypnotics were considered to be the most successful treatment for insomnia (Sivertsen et al., 2009). Similarly, a survey in the United Kingdom into general practitioners' preferences for managing insomnia reported that verbal advice, followed by hypnotics and sedative antidepressants were the preferred treatments for insomnia (Siriwardena et al., 2009). Siriwardena et al. (2009) reported that "GPs felt they had neither sufficient dedicated resources to systematically reduce [hypnotic] prescribing nor were most able to give details of options for pursuing alternative management strategies" (p. 734).

Having the general practitioner equipped to treat insomnia enables insomnia to be managed within the consultation and within the context of the patients' health and social landscape. The established rapport of the general practitioner-patient relationship may also act to enhance the capacity of the general practitioner to influence health behaviours (Moir, van den Brink, Fox, & Hawken, 2009). As mentioned previously, the general practitioner is the most likely health professional to see those with insomnia (Morin, LeBlanc, et al., 2006; Stinson et al., 2006). It is important therefore, that when help is sought, treatment advice can be given. This means having evidence-based treatments that can be implemented in primary care.

#### **1.4 Why the ReFRoSH Study is Needed**

Educating general practitioners and primary care providers regarding evidence-based insomnia treatment is "critical to meeting the unmet needs of numerous patients with insomnia who currently remain undiagnosed and untreated, and to provide patients with alternatives to pharmacologic management of their insomnia" (Troxel & Buysse, 2013, p. 4). What is required is a treatment that is effective, feasible for the general practitioner operating under the constraints and competing pressures of the consultation and acceptable for the patient. The ReFRoSH trial aims to address this unmet need

by assessing the effectiveness of simplified sleep restriction as a brief behavioural intervention for primary insomnia. It is an intervention that could be delivered by the general practitioner during the primary care consultation, and that allows ongoing self-management by the patient.

Cognitive behavioural therapy for insomnia (CBT-I) is effective but its use has been limited due to problems with access and affordability (Irwin, Cole, & Nicassio, 2006; Morin, Bootzin, et al., 2006). As noted by Matteson-Rusby, Pigeon, Gehrman, and Perlis (2010) “the primary barrier to successful treatment of insomnia is the relative unavailability of CBT-I providers” (p. 3). There are few, if any non-pharmacological interventions designed to fit within the primary care consultation. Recently, research has focussed on briefer, more accessible treatments such as abbreviated CBT-I (Edinger & Sampson, 2003) and the behavioural components of CBT-I, sleep restriction and stimulus control, delivered as a brief behavioural treatment for insomnia (BBTI) (Buysse et al., 2011). The aim of the current study was to assess whether an even briefer intervention (“simplified sleep restriction”) designed to fit into two primary care consultations could improve sleep amongst those with primary insomnia.

## **1.5 Thesis Structure**

The thesis is divided into five chapters: Introduction, Literature review, Methods, Results, and Discussion. The Introduction chapter provides the rationale for conducting the study. The Literature review chapter gives the context for the thesis by providing an overview of the pathophysiology of insomnia, a detailed explanation of sleep restriction, a systematic review of sleep restriction for insomnia, and the theory and rationale behind the development of the simplified sleep restriction intervention. The Methods, Results, and Discussion chapters present the development, conduct, results, and implications of the ReFReSH trial.

## **Chapter 2 Literature Review**

This chapter is divided into three major sections. In the first section, the underlying pathophysiology of insomnia is discussed. This provides a context for understanding how non-pharmacological treatments for insomnia exert their effect. In the second section, a systematic review of sleep restriction therapy as a stand-alone treatment for primary insomnia is reported. The final section explains the theoretical basis for the development of the simplified sleep restriction intervention used in the ReFRReSH randomised controlled trial.

### **2.1 The Pathophysiology of Primary Insomnia**

#### **2.1.1 Introduction**

The theoretical rationale for non-pharmacological treatments for insomnia is derived from the conceptual models of normal sleep/wake regulation and from the proposed pathophysiology of insomnia. In order to provide a context for exploring the theoretical rationale the question of “what is good sleep?” is explored. The normal processes of sleep are then outlined. This is followed by a description of the predominant hypotheses of the pathophysiology of primary insomnia. The three most commonly postulated mechanisms are those of “homeostatic dysregulation”, “hyperarousal”, and “circadian dysrhythmia”. The term “homeostatic dysregulation” is used as this the term used in the literature (Pigeon & Perlis, 2006). The empirical evidence underlying these mechanisms is discussed in turn below. The section is concluded by summarising the theoretical rationale for non-pharmacological treatments for insomnia based on the pathophysiological models.

#### **2.1.2 Characteristics of sleep**

##### **“Normal sleep”**

Sleep has been described as “a complex behaviour, one that is organized temporally, responsive to stimuli encountered during wakefulness, and composed of both physiologic and cognitive components” (Spielman, Caruso, & Glovinsky, 1987, p. 541). Good sleep could be defined as that which occurs naturally, without conscious effort, at the appropriate time, and is sufficient to not lead to daytime dysfunction such as fatigue, sleepiness or difficulty with cognitions (American Sleep Disorders Association, 2005).

Sleep in humans is an interplay of three processes: the homeostatic sleep drive, the arousal system, and the circadian rhythm (C. M. Yang, Spielman, & Glovinsky, 2006). Table 2-1 describes these three processes. Homeostatic sleep drive and circadian rhythm interact in the regulation of sleep.

Homeostatic mechanisms strengthen sleep propensity when there has been curtailed sleep and reduce



sleep propensity when there has been excess sleep (Achermann & Borbely, 2011). Thus, the homeostatic drive for sleep increases during waking as sleep pressure or “debt” builds, and decreases during sleep as the sleep debt is paid off (C. M. Yang et al., 2006). The circadian system is independent of sleep and waking. It operates on an approximately 24 hour cycle, is under the control of the biological “clock”, and determines both the timing and propensity of sleep (Czeisler & Buxton, 2011). In addition to the homeostatic sleep drive and the circadian rhythm, sleep onset also requires the arousal system to be dampened sufficient for the normal onset of sleep to be a passive and automatic transition (Espie, 2002).

*Table 2-1: Processes Involved in the Regulation of the Sleep/Wake Cycle*

| <b>Process</b>          | <b>Description</b>  |
|-------------------------|---|
| Homeostatic sleep drive | A process that increases the drive to sleep as hours spent awake accumulate. Sleep deprivation provokes a stronger sleep drive and conversely, oversleeping is followed by a decreased propensity to sleep and shorter or lighter sleeps during subsequent sleep opportunities (C. M. Yang et al., 2006).   |
| Arousal                 | This system promotes wakefulness in opposition to the sleep drive via neuronal groups mainly concentrated within and adjacent to the pontine, midbrain reticular formation, and into the hypothalamus. These neurons synthesise and release a number of neurotransmitters including acetylcholine, serotonin, and noradrenaline to oppose sleep promoting processes (Siegel, 2011). The arousal force can be amplified in various situations, such as stress.   |
| Circadian rhythm        | This is an intrinsic system that generates a biologic rhythm of sleep and wake tendency over approximately a 24 hour period. It is regulated by the interaction of both this internal biological “clock” and associated physiological factors such as body temperature, and by environmental factors such as the light-dark cycle, work patterns and social contacts (these environmental time cues are known as “zeitgebers”) (Czeisler & Buxton, 2011). The primary circadian synchronisers are environmental light-dark schedules. Under ordinary circumstances humans sleep at night in darkness and are awake during the daylight hours (Czeisler & Buxton, 2011). |

Insomnia may be experienced due to derangement in any of these processes. Thus the underlying disruption of the sleep/wake regulation could be due to:

- Homeostatic dysregulation.
- Hyperarousal
- Circadian dysrhythmia

Homeostatic dysregulation refers to the situation where accumulated wakefulness (“sleep pressure”) does not produce the expected easy transition from wakefulness to sleep (Pigeon & Perlis, 2006).

Hyperarousal refers to either an elevated basal level of arousal or a failure to down-regulate arousal at bedtime (Pigeon & Perlis, 2006). Circadian dysrhythmia refers to changes in the timings of the biologic clock that lead to the development of insomnia (such as an erratic sleep schedule or lingering in bed awake). The derangement could either be an inbuilt abnormality or a derangement arising in an otherwise “normal” sleep/wake system due to maladaptive behaviours (C. M. Yang et al., 2006). Inbuilt abnormalities could be an idiopathic tendency towards a weak homeostatic sleep drive, an abnormality in circadian regulation, or a constitutional tendency towards hyperarousal (C. M. Yang et al., 2006). These processes and the maladaptive behaviours that can contribute to insomnia will be discussed subsequently in relation to sleep restriction as a treatment for insomnia.

### **“Good sleep”**

*After a good night’s sleep you rise feeling refreshed and renewed. Your senses soak up simple pleasures, such as the clean smell of the air, the singing of the birds, the texture of the morning paper. You are rested and relaxed but not bored or sleepy. You are interested and pleasantly aware of your surroundings but not overwhelmed. You are engaged with the world. Confident that you are ready to tackle the day ahead, frustrations seem minor, challenges exciting rather than foreboding. You can focus your mind like a laser on any problem, tackle it with exhilaration and confidence, and you can concentrate at the highest level while your body is at rest (Dement & Vaughan, 1999, p. 273).*

In order to provide context to insomnia treatment research, it is helpful to gain a concept of what is meant by “good sleep”. Those with insomnia wish to sleep better (the participants in the current study responded to the study invitation letter specifically for this reason). Ideally, one would imagine they would like to have a good sleep each night. In order to evaluate if a treatment is successful in the eyes of the participant with insomnia, outcome measures must also somehow capture this notion of good

sleep. How do we measure if sleep is “good” or not, especially when insomnia is essentially a subjectively defined complaint? As yet, there is no definitive answer to this question. However, the concept of sleep quality attempts to capture this notion of good sleep. Research recommendations for the evaluation of insomnia treatments suggest an amalgamation of measures in order to capture the experience of sleep from multiple perspectives (Morin, 2003). The concept of sleep quality is explored below. Section 3.6 includes further discussion of the research recommendations for outcome measures used in insomnia treatment research.

### ***Sleep quality***

Sleep quality is a complex clinical phenomenon. To define sleep quality requires recognition of both sleep parameters (for example, sleep duration, time taken to fall asleep, and overnight awakenings) and the subjective perspective of sleep (for example, “restfulness” or “depth”) (Buysse et al., 1989). As noted by Harvey and colleagues “understanding the meaning of sleep quality for individuals with insomnia may turn out to be important for a full recovery from insomnia” (Harvey, Stinson, Whitaker, Moskovitz, & Virk, 2008, p. 384). Despite being a commonly used term in sleep medicine, there is no common definition for sleep quality (Krystal & Edinger, 2008). Studies have attempted to tease out the meaning of sleep quality. These have suggested that sleep efficiency, tiredness on waking and throughout the day, feeling rested and restored on awakening, and the number of awakenings experienced in a night are important aspects of sleep quality (Akerstedt, Hume, Minors, & Waterhouse, 1994; Harvey et al., 2008). The studies have also suggested that sleep quality may have different meanings for different people.

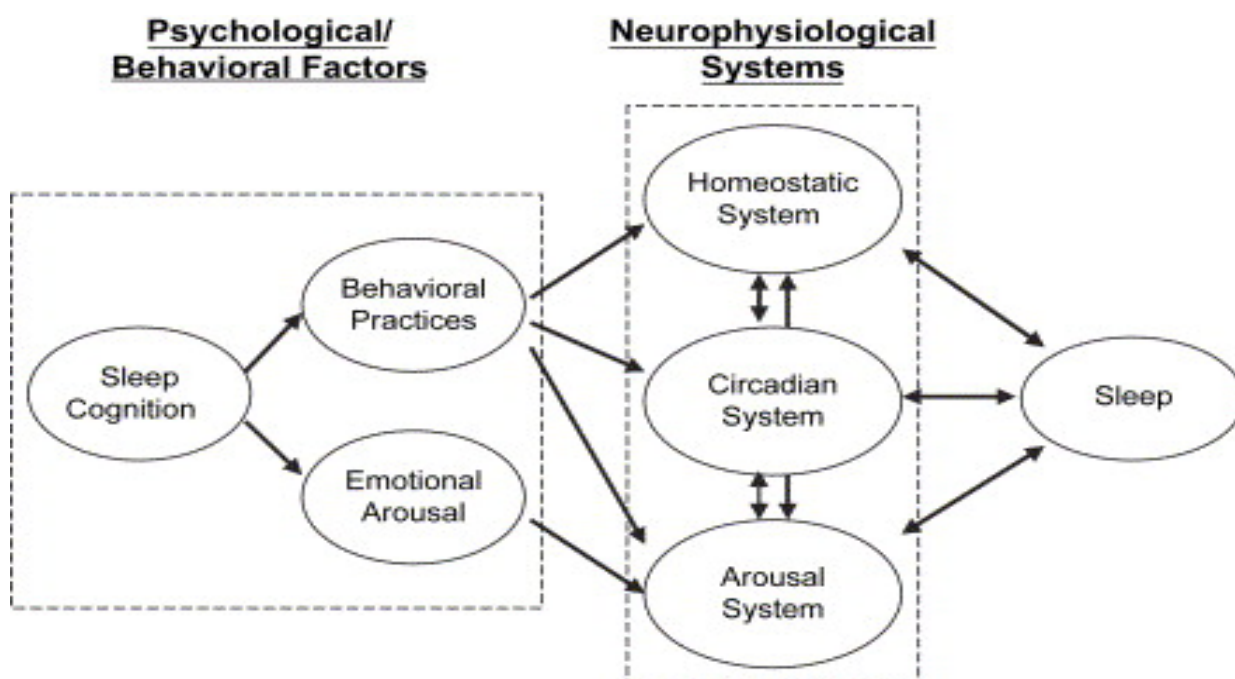
### **Measuring outcomes-the multidimensional nature of insomnia**

In a review of measuring outcomes in randomised clinical trials of insomnia treatments, Morin (2003) concluded that in order to capture the multidimensional nature of insomnia, it is essential to assess treatment effects using multiple outcomes and assessment modalities. This position was reiterated by the recommendations for a standard research assessment of insomnia (Buysse, Ancoli-Israel, Edinger, Lichstein, & Morin, 2006). These recommendations were adhered to, where practicable, in the design of the ReFRReSH trial. Section 3.11 includes a detailed discussion of the outcome measures used in the trial.

### **2.1.3 Models of pathophysiology**

Various models and hypotheses exist for the development and maintenance of insomnia. Despite this, a universally accepted integrated model has yet to be produced (Pigeon & Cribbet, 2012). The physiologic and cognitive behavioural models of insomnia pathophysiology are discussed below. First, the physiologic model is presented. This provides empiric evidence for the disruption of the normal

sleep processes by way of *homeostatic dysregulation*, *hyperarousal*, and *circadian dysrhythmia*. This relates to the concept of normal sleep/wake regulation and represents the idea that insomnia is a disruption of the normal processes of sleep. Other models have been developed that emphasise the cognitive and behavioural aspects of insomnia. These include the “3 P model” of insomnia, the “stimulus control model”, the “cognitive model”, insomnia as an interaction between sleep-interfering and sleep-interpreting processes, the “psychobiological inhibition model”, and the “attention-intention-effort pathway”. Each of these models is discussed in turn below. To navigate the spectrum of theories presented and how they might relate to each other, it is useful to refer to an overarching conceptual model proposed by Yang, Spielman and Glovinsky (2006) shown in Figure 2-1 below.



*Figure 2-1: Conceptual model shows that psychological/behavioural factors influence sleep through the mediation of the neurophysiologic regulation of normal sleep.*

From "Nonpharmacologic strategies in the management of insomnia," by C.M. Yang, A.J. Spielman, and P. Glovinsky, 2006, *Psychiatric Clinics of North America*, 29(4), 895-919. Copyright (2006), by Elsevier. Reprinted with permission.

### **Physiological models**

Homeostatic dysregulation, hyperarousal, and circadian dysrhythmia represent interruption of the normal sleep systems. The evidence for each of these system derangements are presented separately.

However, it is likely that the development of insomnia is often an interaction between the three system derangements (C. M. Yang et al., 2006).

### ***Homeostatic dysregulation***

When sleep homeostasis is considered intact (“steady state”), a sleep deficit elicits a compensatory increased intensity and duration of sleep (Achermann & Borbely, 2011; Borbely, 1982). In the review by Pigeon and Perlis (2006), several lines of evidence have been proposed to support the notion that homeostatic dysregulation may be an underlying mechanism in the aetiology of primary insomnia. The basic reasoning is that in those with insomnia the duration of wakefulness is normal, but the consequent effortless transition to a consolidated, deep sleep does not occur. Therefore, Pigeon and Perlis (2006) have hypothesised that there must be dysregulation in the sleep homeostat. The small body of available evidence for this relates to differences seen when those with primary insomnia are compared to “good sleeper” controls. The data suggest that those with primary insomnia have a deficiency of slow wave sleep, have normal to reduced levels of daytime sleepiness despite sleep loss and complaints of fatigue, show sleepiness after sleep deprivation, and show a response to sleep restriction therapy (Pigeon & Perlis, 2006). These lines of evidence are discussed in turn below.

### ***Slow wave sleep deficiency***

The deeper stages of sleep (stages 3 and 4) seen on the electroencephalograph (EEG) are commonly referred to as slow wave sleep. The level of slow wave sleep activity on the EEG correlates to sleep depth or intensity and is determined by the duration of prior sleep and waking (Achermann & Borbely, 2011). Despite some inconsistent findings, research has demonstrated deficient slow wave sleep in those with chronic primary insomnia (Frankel, Coursey, Buchbinder, & Snyder, 1976; Gaillard, 1978; Pigeon & Perlis, 2006; Reynolds et al., 1984). This is in contrast to what would be expected, where sleep deficit should produce increased slow wave sleep activity if the sleep homeostat is intact. To help resolve the inconsistency seen with research concentrating on slow wave sleep, Pigeon and colleagues proposed measuring sleep homeostasis using slow wave sleep latency (minutes to achieve slow wave sleep from sleep onset) (Pigeon & Perlis, 2006). This was a preliminary study on a small number of participants ( $n = 33$ ), which showed patients with primary insomnia had longer slow wave sleep latencies than controls despite having similar amounts of slow wave sleep. These findings were proposed to be consistent with the perspective that sleep homeostasis may be altered in patients with primary insomnia (Pigeon & Perlis, 2006). Possible mechanisms proposed for the association between deficient slow wave sleep and insomnia include the slow wave sleep deficiency itself being sufficient to induce homeostatic imbalance (if, for example, slow wave sleep has a role in sleep induction and maintenance), or that the slow wave sleep deficiency (or slow wave sleep latency) may leave sleep

more susceptible to endogenous or external disruption (that is, lighter sleep confers a higher chance of being awoken due to minor disturbing influences) (Frankel et al., 1976).

### *Level of daytime sleepiness*

By definition, insomnia involves disrupted sleep that is non-restorative or of poor quality (American Sleep Disorders Association, 2005). It would be expected, therefore, that those suffering from insomnia would exhibit daytime sleepiness as a consequence of this sleep loss due to compensatory increase in sleep drive (that is, assuming sleep homeostasis is intact) (Pigeon & Perlis, 2006). Sleepiness is often measured using the multiple sleep latency test (MLST) (Carskadon & Dement, 1977; Richardson et al., 1978). The MLST is a measure of the ability or tendency to fall asleep based on the assumption that with increased sleepiness, there is a decrease in the time taken to fall asleep (M. R. Littner et al., 2005). Studies have shown that those with chronic insomnia have normal or longer than normal time taken to fall asleep (normal or long MLST scores) rather than short MSLT scores which would be expected as a reflection of sleep deprivation (Bonnet & Arand, 1995; Dorsey & Bootzin, 1997; Mendelson, Garnett, Gillin, & Weingartner, 1984; Seidel et al., 1984; Stepanski, Zorick, Roehrs, Young, & Roth, 1988). Pigeon and Perlis make the point that although this is often cited as evidence for hyperarousal in those with insomnia; it may be that this finding is actually related to homeostatic dysregulation (Pigeon & Perlis, 2006). They further speculate that this may represent that those with insomnia require more than normal levels of sleep deficit to initiate the compensatory increase in sleep drive that would be expected from the innate sleep homeostasis system (Pigeon & Perlis, 2006).

### *Sleepiness following sleep deprivation*

When patients with primary insomnia are experimentally sleep deprived such as in the study by Stepanski et al (Stepanski, Zorick, Roehrs, & Roth, 2000), they do show an increased sleepiness as represented by shorter MSLT scores. The increased sleepiness from baseline was comparable to that shown in the group of good sleepers following sleep deprivation (Stepanski et al., 2000). This suggests that although sleep homeostasis is compromised in patients with primary insomnia, it is intact, and that only a very strong challenge to the system provokes the normal homeostatic response of appropriately increased sleepiness following sleep deprivation (Pigeon & Perlis, 2006). That is, rather than sleep deficits in those with primary insomnia not provoking a compensatory increase in deep sleep to restore homeostatic balance, a larger than usual sleep deficit is required in order to cause the compensatory increase in deep sleep. Therefore, the mechanism of sleep homeostasis is intact in those with primary insomnia, but it works in a slightly different fashion than in “normal” sleepers.

### *Response to sleep restriction treatment*

Several small studies have indicated that sleep restriction treatment may result in an increase in slow wave sleep. One study found a significant increase in slow wave sleep over time in a group treated with partial sleep restriction ( $n = 11$ ) where time in bed was reduced by only 30 minutes for the duration of the study (Hoch et al., 2001). However, this study was in a group of rest home residents and not in those with primary insomnia. Another study compared elderly patients with primary insomnia randomised into sleep compression (where sleep is progressively reduced until normal efficiency is achieved), relaxation therapy, or placebo groups (Lichstein, Riedel, Wilson, Lester, & Aguillard, 2001). At one year of follow up the sleep compression group exhibited a modest increase in slow wave sleep and slow wave sleep percentage. No changes were observed in the other groups. A further study evaluated a group of nine patients with primary insomnia after eight weeks of cognitive behavioural therapy for insomnia (which included restricting sleep) (Cervena et al., 2004). This study also demonstrated an increase of slow wave sleep; however, there was no increase in slow wave sleep percentage as total sleep time was also increased. This study was limited by the lack of an insomnia control group. Although none of these studies are able to give irrevocable evidence that restricting sleep (or “sleep restriction therapy”) increases slow wave activity (and thus inferred improvement in quality), together they support the hypothesis that sleep restriction may enhance sleep pressure and improve homeostatic sleep regulation by increasing slow wave activity (Cervena et al., 2004). They also appear to support the notion that in insomnia, the sleep homeostat is intact but perhaps is insufficiently activated at lower levels of sleep deficit (Pigeon & Perlis, 2006).

### ***Hyperarousal***

Evidence of significant physiological differences between “good sleepers” and “poor sleepers” were reported in the 1960’s by Monroe (1967). These differences were demonstrated in the pre-sleep period as well as throughout the night (Monroe, 1967). Since then, physiologic, cortical, and cognitive differences have been demonstrated in those with insomnia showing that those with insomnia have demonstrable levels of hyperarousal compared to controls (Bonnet, 2010). For example, those with insomnia have been demonstrated to have: elevated heart rate, increased sympathetic nervous system activity (“fight or flight”), and increased hypothalamic-pituitary-adrenal axis (stress hormone cascade) activity (*physiologic hyperarousal*). They have also shown changes in brain electrical activity measured by electroencephalograph (*cortical hyperarousal*). Those with insomnia have also shown increased levels of anxiety and sleep-related worries (*cognitive hyperarousal*). These differences have been interpreted as evidence that hyperarousal may be a key mechanism contributing to the occurrence of insomnia whereby the normal processes of sleep are overridden or “masked” by the levels of arousal (Bonnet, 2010). This has further been conceptualised as being either an elevated basal level of arousal or as a failure to appropriately down-regulate normal levels of arousal at night (Nofzinger et al., 2004;

Pigeon & Perlis, 2006). There is also some evidence that hyperarousal may reflect a primary central nervous system state rather than solely being a secondary effect of sleep disturbance (Bonnet & Arand, 1996). The physiologic, cortical, and cognitive dimensions of hyperarousal are discussed in turn below.

### *Physiologic hyperarousal*

Individuals with insomnia have been shown to have a number of markers of increased sympathetic nervous system activity such as increased levels of circulating catecholamines (Vgontzas et al., 1998), increased basal metabolic rate (Bonnet & Arand, 1995), elevated heart rate (Bonnet & Arand, 1998), increased body temperature during night-time wakefulness (Lushington, Dawson, & Lack, 2000), and an increased level of central nervous system metabolic rate (Nofzinger et al., 2004). Adding weight to this theory of hyperarousal, normal or prolonged multiple sleep latency test scores have also been demonstrated in those with primary insomnia compared to normal sleepers this suggests that those with insomnia are not excessively sleepy during the day despite poor sleep at night (Bonnet & Arand, 1995; Stepanski et al., 1988). These results support the existence of a tendency towards physiologic hyperarousal in those with primary insomnia (Bonnet, 2010).

A central feature of the physiologic hyperarousal seen in primary insomnia is the levels of increased corticotropin-releasing factor (CRF) activity and hypothalamic-pituitary-adrenal (HPA) axis over-activity (Buckley, Schatzberg, Buckley, & Schatzberg, 2005; Richardson & Roth, 2001; Vgontzas et al., 2001). The increased CRF activity and HPA over-activity has in turn been hypothesised to arise from either a genetic predisposition or as a consequence of early stress experiences; resulting in an exaggerated response to stress (Richardson & Roth, 2001). The HPA axis is involved in the secretion of CRF which acts on the anterior pituitary to secrete adrenocorticotrophic hormone (ACTH), which stimulates cortisol release from the adrenal cortex in response to stress (Huether, 1996). Increased cortisol secretion leads to arousal, sleeplessness, and increased nocturnal awakenings. Sleep disruption also leads to changes in cortisol secretion. Studies have shown that:

- increased evening and nocturnal plasma cortisol levels correlate with arousal, sleeplessness, and increased nocturnal awakenings (Rodenbeck, Huether, Ruther, & Hajak, 2002).
- those with primary insomnia have been shown to have higher levels of ACTH and cortisol than controls throughout the 24 hour sleep/wake cycle (Rodenbeck et al., 2002; Vgontzas et al., 2001; Vgontzas et al., 1998).

An alternate explanation is that the negative emotions produced by disturbed sleep may lead to an increase in HPA activity, thus disrupting sleep further and leading to entrenched primary insomnia with persistent difficulty sleeping (Richardson & Roth, 2001; Rodenbeck et al., 2002). This interaction between insomnia, arousal, and cortisol is shown in Figure 2-2.



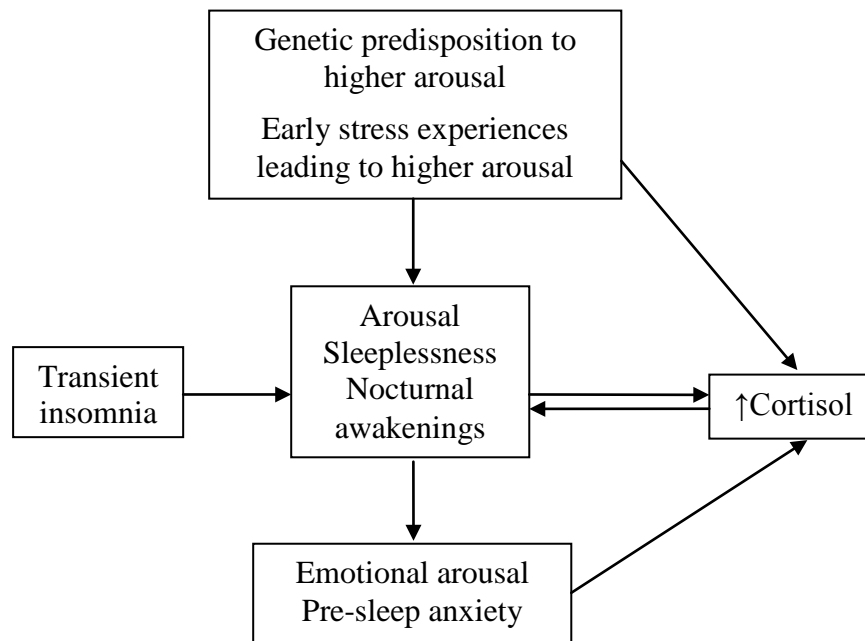


Figure 2-2: The cycle of increased cortisol secretion and sleep disruption seen in primary insomnia

### *Cortical hyperarousal*

Cortical hyperarousal may also be an explanatory mechanism for the sleep disturbances experienced by those with primary insomnia and forms the basis of the neurocognitive model of insomnia (Perlis, Giles, Mendelson, Bootzin, & Wyatt, 1997). The neurocognitive model suggests that as one develops chronic insomnia (via stressors leading to maladaptive behaviours), classical conditioning that normally elicits relaxing responses (for example, bedroom or bed cues) now elicit high frequency EEG activity (arousal) (Perlis et al., 1997). For example, for those with insomnia lying in bed may become stressful as the worries of not being able to sleep and how it might impact the coming day occupy the mind. An association is formed between lying in bed and feeling stressed and anxious. Therefore, each time one gets into bed, the stressful feelings and anxieties are triggered due to this conditioned response. This conditioned cortical arousal persists even when the situational reason for the insomnia has abated (Perlis et al., 1997). For example, the insomnia may have started with the stress of exams. A conditioned response may develop associating bed as a place of stress, anxiety, and consequent cortical arousal (increased high frequency brain wave activity). The exam period finishes, background stress levels returned to normal, but the conditioned association between the bed and arousal persists, meaning that the problems with insomnia persist.

The conditioned arousal increases information processing and memory formation during these situations which makes those with insomnia vulnerable to disturbance by various stimuli (for example, environmental), results in insomnia complaints (Perlis et al., 1997). What this means is that for someone who has “bed” associated with arousal and increased high frequency brain wave activity; the brain is more alert to noises outside, and around the house, to cold feet, and a softly snoring partner. It is this noticing and processing of stimuli (usually dampened in the period just before falling asleep) that further “wakes up” the brain and prevents the complainant from sleeping (Perlis et al., 1997). The evidence to support this hypothesis relates to research suggesting that those with insomnia have higher levels of high frequency electroencephalographic (EEG) activity in the beta (14-32 Hz) and gamma (>32 Hz) ranges both at sleep onset and during sleep than controls (Freedman, 1986; Merica, Blois, & Gaillard, 1998; Merica & Gaillard, 1992; Perlis, Smith, Andrews, Orff, & Giles, 2001).

These high frequency EEG patterns are associated with cognitive function and are thought to reflect information processing and/or memory formation (Perlis et al., 1997; Pulvermuller, Lutzenberger, Preissl, & Birbaumer, 1995; Spydell & Sheer, 1982; Tiitinen, May, & Naatanen, 1997). Normally, there is no recall of information immediately prior to sleep nor throughout the night (including brief arousals) (Bonnet, 1983; Koukkou & Lehmann, 1968; Lasaga & Lasaga, 1973; Lehmann & Koukkou, 1974; Perlis et al., 1997; Portnoff, Baekeland, Goodenough, Karacan, & Shapiro, 1966; Wood, Bootzin, Kihlstrom, & Schachter, 1992; Wyatt, Bootzin, Anthony, & Bazant, 1994). When these functions are not attenuated prior to sleep (as would occur in the normal transition into sleep) the distinction between wakefulness and sleep is blurred leading to the judgment or “attribution” of sleep quality becoming impaired (Perlis et al., 1997). It is thought that this cortical and cognitive arousal may explain the tendency for those who suffer from insomnia to overestimate the time it takes them to fall asleep and the amount of time that they spend awake during the night (Perlis et al., 1997).

The theory of cortical hyperarousal is further supported by the work of Yang and Lo (2007) who investigated the processing of auditory information during sleep through the measurement of event-related potentials. Event-related potentials can show neurophysiologic activity elicited by sensory stimulation; in this case by auditory pure tones (C. M. Yang & Lo, 2007). The abnormal event-related potential changes seen in those with insomnia were thought to reflect an impairment in the sleep protecting inhibitory mechanism that prevents sensory events during sleep provoking cognitive or cortical arousal (C. M. Yang & Lo, 2007). This work was expanded upon by Hairston and colleagues who tested event-related potential sensory gating of information during sleep and also found that those with primary insomnia had an impairment in the ability to filter out external sensory information during sleep contributing to night time arousal (Hairston, Talbot, Eidelman, Gruber, & Harvey, 2010). Evidence also suggests there may be an inhibitory malfunction in the sleep/wake mechanism of the

hypothalamus leading to an inability of the arousal system to downregulate for sleep (Pigeon & Perlis, 2006).

Functional neuroimaging studies have shown higher cerebral glucose metabolism in both waking and sleep states in those with insomnia (Nofzinger et al., 2004). The increased brain metabolism seen in those with primary insomnia was correlated with increased overnight awakenings (Nofzinger et al., 2006). There was also evidence of a failure of the wake-promoting structures of the brain to show attenuation in metabolism in the transition to sleep (Nofzinger et al., 2004). This suggests that the higher cerebral metabolism seen in the non-rapid eye movement (NREM) sleep states may be due to a lack of reduction in activity of these areas in the progression from wake to sleep (Nofzinger et al., 2004). Increased cortical arousal has also been indicated by studies showing increased levels of “cyclic alternating patterns” during the night in those with insomnia (indicating unstable sleep) (Terzano et al., 1985; Terzano et al., 2003). Further to this, reductions in  $\gamma$ -aminobutyric acid (GABA), the main inhibitory neurotransmitter in the brain, have been shown in those with primary insomnia suggesting less inhibition (and therefore more neurotransmitter activation) (Winkelman et al., 2008). However, the role of GABA in the aetiology of chronic insomnia has yet to be fully elucidated (Plante, Jensen, & Winkelman, 2012).

### *Cognitive hyperarousal*

In contrast to the physiological arousal discussed above, cognitive hyperarousal relates to various negatively-toned thoughts and beliefs that prevent the natural transition into sleep via activation of the sympathetic nervous system (Harvey, 2002). That is, worrying can lead to increased arousal and difficulty sleeping. Some psychological research has profiled the person prone to insomnia may be somewhat anxiety-prone with a ruminative tendency who tends to have more negatively toned cognitions than those of good sleepers (Borkovec, Lane, & VanOot, 1981; Freedman & Sattler, 1982; Harvey, 2002; Morin, 1993; Van Egeren, Haynes, Franzen, & Hamilton, 1983). Insomnia sufferers report more difficulty coping with daily stressors, perceive their lives as more stressful with more unpredictable and uncontrollable situations, and appraise their sleep as more unpredictable and uncontrollable than good sleepers (Gallup Organisation, 1991; Morin, 1993; Morin, Blais, & Savard, 2002; Morin et al., 2003). This mental activity at bedtime is associated with disruption of sleep (Espie, 2002; Harvey, 2000; Lichstein & Rosenthal, 1980; Nicassio, Mendlowitz, Fussell, & Petras, 1985). Increased cognitive arousal, especially when negatively toned may also lead to physiological hyperarousal (Morin, 1993; Van Egeren et al., 1983). It has also been suggested that believing insomnia is harmful can contribute to insomnia persistence (Jansson & Linton, 2007).

The characteristics noted above help explain the experience of the person with insomnia and the cycle that is often created where poor sleep and daytime consequences increase pre-sleep worry and arousal contributing to further difficulty with sleep and a perpetuation and escalation of the cycle of insomnia (Morin, 1993; Perlis, Smith, & Pigeon, 2005). An alternative perspective is that cognitive arousal may be an “epiphenomenon” of night time wakefulness where the wakefulness is the initial difficulty creating the space for intrusive cognitions to cause further disruption (Freedman & Sattler, 1982; Harvey, 2002; Morin, 1993).

### *Circadian dysrhythmia*

The circadian system has a key role in the regulation of the sleep/wake cycle in humans (Section 2.1.2). The circadian pacemaker (or “biological clock”) confers an endogenous rhythmicity with a period that is close to 24 hours (Czeisler et al., 1999). The underlying timing of the circadian pacemaker is genetically conferred but is synchronised primarily by environmental light-dark schedules (Czeisler & Buxton, 2011).

A circadian rhythm that has become desynchronised may lead to insomnia. For example, maladaptive habits of those with insomnia such as going to bed early, sleeping in after a poor night’s sleep, or exposure to light during the sleep period may contribute to circadian dysrhythmia without an inherent defect in the circadian system (Perlis, Smith, et al., 2005). Sleep may be attempted at a time that is not in keeping with the circadian readiness for sleep, further contributing to sleep difficulties. An example of this is to consider the body’s thermoregulation as a marker of circadian rhythmicity. Endogenous core body temperature shows circadian rhythmicity following a near sinusoidal pattern (Lack, Gradisar, Van Someren, Wright, & Lushington, 2008). Sleep propensity is highly correlated to core body temperature; people tend to sleep when the core body temperature is low and tend to be more awake when the core body temperature is high (T. Roth, 2004). Sleep is typically initiated as the temperature is on the downward gradient, about five to six hours before the temperature minimum, which normally occurs between 4am and 6am (Campbell & Broughton, 1994; Czeisler et al., 1980; Krauchi & Wirz-Justice, 1994; Lack et al., 2008).

Surrounding this region of high sleep propensity are periods of low sleep propensity or increased wakefulness. This has been termed the “wake maintenance zone” (Strogatz, Kronauer, & Czeisler, 1987b, p. R173) or the sleep “forbidden zone” (Lavie, 1986, p. 414). The early evening wake maintenance zone occurs six to nine hours before the body temperature minimum and a second, less pronounced zone of increased wakefulness occurs about four to seven hours after the body temperature minimum (Dijk & Czeisler, 1994; Klein et al., 1993; Strogatz et al., 1987b; Zulley, Wever, & Aschoff, 1981). Therefore, sleep duration is partially dependent on the phase of this temperature rhythm the

individual selects as bedtime (Sewitch, 1987). Those with sleep onset insomnia have been found to have delayed temperature rhythms, thus, bedtimes were found to be coinciding with the wake maintenance zone (Morris, Lack, & Dawson, 1990). It has also been suggested that early morning awakening insomnia arises from phase advanced circadian rhythms, which evoke early arousals from sleep (Lack, Mercer, & Wright, 1996). In this situation, sleep cannot be re-initiated as awakening has occurred in the zone of increased wakefulness. From a treatment point of view, re-synchronising (or re-entrainment of) the circadian rhythm has the potential to improve sleep quality and efficiency. A summary of the contributing factors leading to insomnia is presented in Figure 2-3.

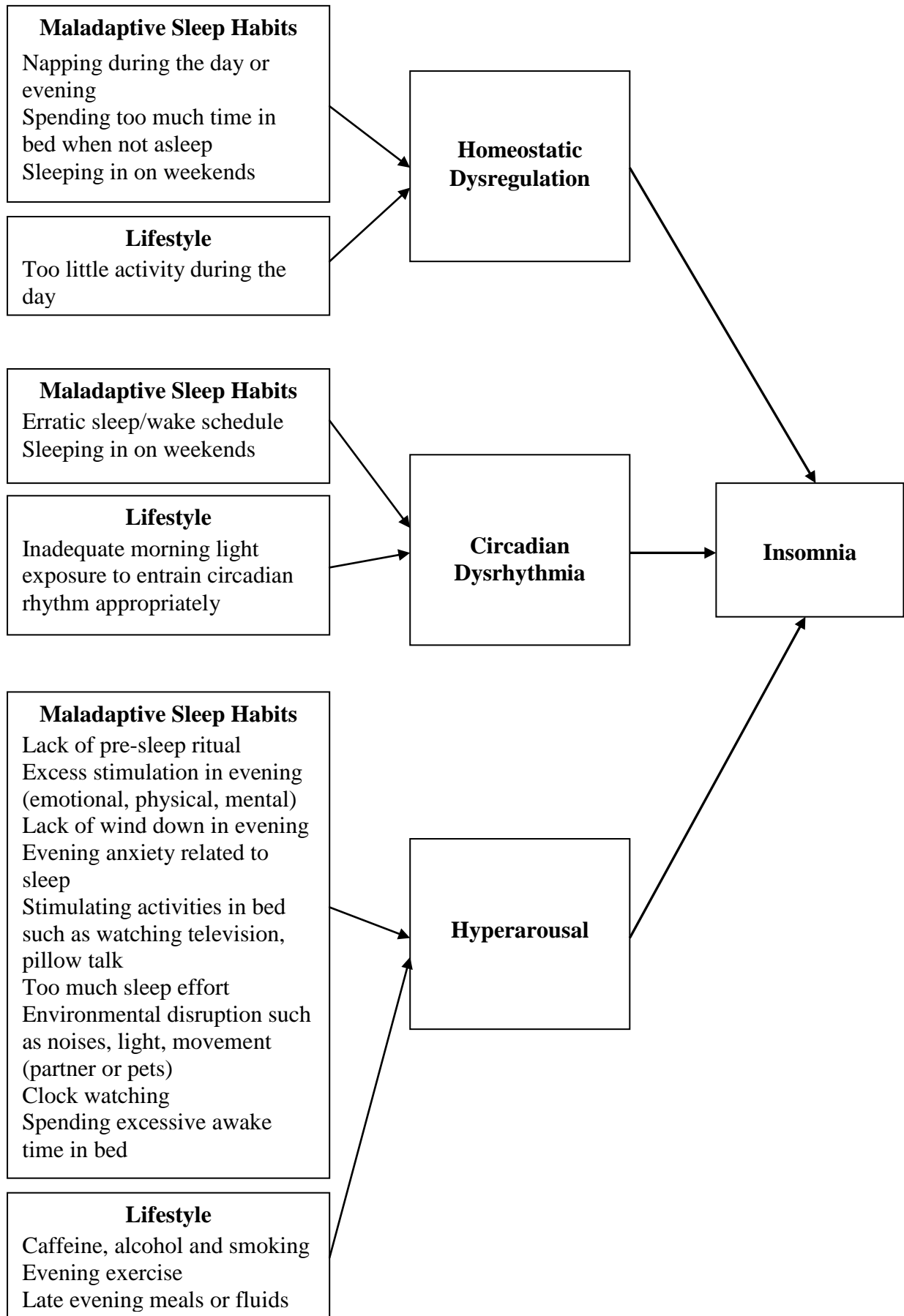


Figure 2-3: The influence of behavioural factors on the physiological processes of sleep leading to insomnia

## **Cognitive behavioural models**

Several cognitive behavioural models have been proposed to understand the factors and mechanisms involved in the maintenance of insomnia (Espie, 2002; Espie, Broomfield, MacMahon, Macphee, & Taylor, 2006; Harvey, 2002; Lundh & Broman, 2000; Spielman, Caruso, et al., 1987). These models all similarly emphasise the major role and interconnectedness of cognitive, affective, behavioural, and physiological factors in maintaining insomnia (Jansson & Linton, 2007).

### ***The “3 P model” of insomnia***

A useful behavioural model of insomnia was proposed by Spielman et al. (Spielman, Caruso, et al., 1987). The “3 P model” of insomnia conceptualises the factors involved in insomnia into temporal groups, suggesting that three distinct elements account for the onset and course of insomnia: predisposing, precipitating, and perpetuating factors (Glovinsky & Spielman, 2006). Within this construct, predisposing factors are the underlying characteristics that render an individual prone to insomnia, the precipitating events are those that can be identified at the time sleeplessness became acute, and the perpetuating factors are those maladaptive attitudes and practices that come into play as the individual with poor sleep struggles to cope with the problem. As can be seen in Figure 2-4, for the person with an underlying predisposition to insomnia, a relatively mild additional influence of a precipitating factor (acute trigger) could cause the person to cross the insomnia threshold. Table 2-2 gives examples of insomnia predisposing, precipitating, and perpetuating factors. The perpetuating factors are those described in the cognitive behavioural models presented below. These factors may help explain why some may people develop chronic insomnia while others remain good sleepers in the face of similar predisposing and precipitating factors.

*Figure 2-4: The “3 P model” of insomnia: Factors contributing to the development of insomnia*

From *Case Studies in Insomnia* (p. 12), edited by P. J. Hauri, 1991, New York: Plenum Publishing Corporation. Copyright [1991] Plenum Publishing Corporation. *Image not available for electronic open access version of thesis.*

*Table 2-2: Factors Associated with the Development and Persistence of Insomnia*

| <b>Predisposing</b>  | <b>Precipitating</b>  | <b>Perpetuating</b>  |
|--|---|--|
| Homeostatic dysrhythmia  | Change in daytime level of activity e.g. retirement, holidays     | Excessive time spent in bed<br>Napping<br>Reduced daytime level of activity<br>Irregular sleep schedules   |
| Hyperarousal<br>(Including personality traits associated with sustained level of arousal e.g. perfectionism) | Stressful events<br>Intense positive or negative emotional events | Increased caffeine<br>Worry about sleep or daytime impaired function<br>Conditioning between bedtime cues and arousal<br>Bedtime television, iPad and iPhone use |
| Circadian dysrhythmia  | Changes in sleep/wake schedule e.g. shift work, jet lag, holidays | “Sleeping in” at weekends or after a poor night’s sleep  |

*Note.* Adapted from Spielman, Caruso, and Glovinsky (1987) and Yang, Spielman, and Glovinsky (2006).



As well as explaining the development and persistence of insomnia, the 3 P model helps to guide the treatment process and aids in the understanding of how both cognitive and behavioural treatments exert their effect. Using this explanatory model, perpetuating factors have a dominant role in the chronicity of insomnia. The theory that excessive time spent in bed is a major force that perpetuates insomnia is at the core of the proposition that chronic insomnia can be addressed by restricting time in bed (Spielman, Saskin, & Thorpy, 1987). The 3 P model can also be used to explain the effect of cognitive behavioural therapy for insomnia whereby the precipitating and perpetuating factors are targeted using both cognitive and behavioural strategies (Espie, 2007).

### ***The “stimulus control model” of insomnia***

The stimulus control model was proposed by Bootzin, Epstein, and Wood (1997). It is based upon the principle of operant conditioning whereby a stimulus can elicit a variety of responses, and the particular response elicited depends upon the “conditioning history” (Talbot & Harvey, 2010). Bootzin et al. (1997) proposed that in the individual with insomnia, the bed and bedroom have become cues for arousal rather than sleep. This has occurred because those with insomnia have engaged with non-sleep activities in the bed and bedroom (such as watching television, talking on the telephone, worrying). Therefore, “sleep stimuli” (bed time, bed, or bedroom) have been paired with other activities instead of specifically being paired with sleep. This new association is called a conditioning history. As a consequence of insomnia, the sleep stimuli can also become a cue for anxiety and frustration creating arousal, which also prevents sleep (Bootzin, Epstein, & Wood, 1991; Talbot & Harvey, 2010). Stimulus control therapy is based on this theoretical model. It aims to re-establish the bed time, bedroom, and bed as strong conditioned cues for sleep.

### ***The “cognitive model” of insomnia***

A cognitive model has been developed by Harvey to provide a conceptual framework for the development of insomnia (Harvey, 2002). Implicit in this model is that the sleep deficit is a consequence of cognitive processes rather than being a deficit in the endogenous sleep/wake cycle (Harvey, 2002). The cognitive model focuses on the excessively negatively-toned cognitive activity found in those with chronic insomnia. It suggests that this cognitive activity triggers both autonomic arousal and emotional distress. This anxious state then triggers selective attention and monitoring of “sleep-related threats” such as internal or external indicators that enough sleep is not being achieved in order to function well the next day (Harvey, 2002). Any detection of these indicators leads to further worry and concern culminating in a distorted perception of sleep difficulty and overestimation of sleep deficit and daytime impaired function (Harvey, 2002). The consequence of this process is an escalation in anxiety that then leads to a real deficit as these prevailing cognitions are incompatible with sleep onset. The model also suggests that both daytime and night time processes are of equal importance.

That is, negative cognitions during the day feed into the night time insomnia. This may involve negatively-toned cognitive activity such as being pre-occupied with feeling tired and not performing adequately, or beliefs such as eight hours of sleep and “super alertness” during the day are necessary representations of having had an adequate sleep (Harvey, 2002). This model suggests that interventions targeting cognitive processes would help to reduce insomnia symptoms and restore normal sleep patterns.

### ***Insomnia as an interaction between sleep-interfering and sleep-interpreting processes***

Lundh and Broman (2000) have proposed that insomnia is an interaction between sleep-interfering and sleep-interpreting processes. They use the distinction between these two processes as a way of organising existing theories about the aetiology of insomnia. In their integrative model, vulnerability factors for sleep-interfering arousal processes are: arousability, stimulus-arousal associations, behavioural and cognitive strategies with regard to the sleep situation, and emotional aspects of interpersonal relations (Lundh & Broman, 2000). These factors lead to arousal (physiological, emotional, and cognitive), which then disrupt sleep. Vulnerability factors for dysfunctional sleep-interpreting processes are suggested to be: high personal standards concerning sleep and daytime functioning, dysfunctional beliefs about sleep needs and the consequences of poor sleep, and attributions of poor sleep and daytime functioning (Lundh & Broman, 2000). These dysfunctional sleep-interpreting processes are suggested to either directly lead to insomnia due to how sleep and daytime functioning has been appraised, or that this appraisal leads to arousal which then affects sleep (Lundh & Broman, 2000). Lundh and Broman argue that it is important to distinguish between the two processes as it should guide the emphasis of treatment. For example, if sleep-interfering processes dominate, treatments such as relaxation, stimulus control, and sleep restriction may be appropriate treatments; and where sleep-interpreting processes dominate, cognitive methods might be more appropriate (Lundh & Broman, 2000; Talbot & Harvey, 2010). Where both processes are involved, both kinds of treatment approaches may be required (Lundh & Broman, 2000).

### ***The “psychobiological inhibition model” and the “attention-intention-effort pathway”***

The psychobiological inhibition model of insomnia was proposed by Espie (2002) to integrate the various explanations of insomnia into a conceptual framework. Within this framework insomnia is proposed as “a persistent loss of expression of normal sleep” where good sleep is regarded as the default state (Espie, 2002, p. 229). This is proposed to occur via inhibition of the normal processes of sleep either by way of inhibition of normal sleep homeostasis, circadian timing, or the automaticity and plasticity of sleep (or capability to “absorb and readjust”) (Espie, 2002, p. 226). The psychobiological inhibition model presumes both an underlying ability to exhibit normal sleep and an interaction between physiological, cognitive, affective and behavioural sleep-influencing factors. Relating this

model to that of the hyperarousal model mentioned earlier, Espie's theory suggests it is inhibition of the normal de-arousal process necessary for normal sleep that is impaired, rather than there being a state of excitation (hyperarousal) (Espie, 2002). He does not propose that physiological hyperarousal does not occur, but that this may be a distinct subtype of insomnia. Furthermore, Espie suggests that de-arousal is considered as the reliable correlate of good quality sleep (Espie, 2002). Espie's psychobiological inhibition model suggests "good sleep is a function of an unimpeded de-arousal process that permits homeostatic and circadian imperatives to engage sleep automatically" (Espie, 2007, p. s6). The model also proposes that insomnia may be caused by the heightened arousal resulting from deliberately trying too hard to sleep.

Espie, Broomfield, MacMahon, Macphee, and Taylor (2006) further refined this idea by proposing an attention-intention-effort pathway whereby persistent insomnia is the result of selective attention bias to sleep, an active intention to sleep, and effort engaged to fall asleep (Espie, 2007; Espie et al., 2006). They proposed considering primary insomnia as a "sleep effort syndrome" (Espie et al., 2006). The foundation for this argument is that normal sleep is an automatic process and that focused attention and effort to control its expression inhibit this inherent automaticity leading to insomnia (Espie et al., 2006). The first step in this pathway is a preoccupation that develops towards sleep ("sleep-related attention bias"). This is proposed to inhibit the automaticity of sleep much like the example provided by Espie et al. (2006) whereby one may be able to run down a flight of stairs with ease, but if one was asked to focus on consciously controlling one's legs whilst descending, the task would be significantly more difficult. The second step proposed in this pathway involves developing an explicit intention to sleep and the underlying psychological theory whereby consciously striving (intending) to produce a desired behavioural goal can be inhibiting. The good sleeper can thus be thought of as "abandoning wakefulness" rather than trying to fall asleep (Espie et al., 2006). In those with insomnia, the attention and explicit behavioural action (intention) of trying to fall asleep further inhibits the automaticity of sleep. The final step in this pathway is where increased effort to fall asleep increases arousal and effortful preoccupation with sleep ("sleep effort") (Espie et al., 2006). The attention-intention-effort pathway in this model suggests that treatment options including cognitive and behavioural elements to modify these processes may reduce insomnia symptoms and restore normal sleep processes (Talbot & Harvey, 2010).

## **2.2 Insomnia Treatment Options**

The preceding section discussed the underlying theoretical models for the development and persistence of insomnia. These models highlighted the interplay of behavioural, cognitive, affective, and physiological factors in the development and persistence of insomnia. The models also provided a context for understanding the methods of insomnia treatment and how sleep restriction may exert its effect. The current section provides further context for the investigation of sleep restriction therapy in the primary care setting by giving an overview of the available evidence regarding effective treatments for insomnia and highlighting the gaps in knowledge that exist. This is followed by a discussion of the inability for insomnia treatment recommendations to make the widespread transition into primary care everyday practice. The section is concluded with a detailed explanation of sleep restriction encompassing its background and theoretical rationale as a treatment for insomnia.

### **2.2.1 Cognitive behavioural treatments**

The American Academy of Sleep Medicine (AASM) published Practice Parameters for the Psychological and Behavioural Treatment of Insomnia in 2006 which supported the effectiveness of psychological and behavioural treatments for chronic insomnia (Morgenthaler et al., 2006).

Empirically-supported treatments include: cognitive behavioural therapy, sleep restriction, stimulus control therapy, relaxation training, and paradoxical intention (Morin, Bootzin, et al., 2006).

Table 2-3 summarises these treatments. Cognitive behavioural therapy for insomnia (CBT-I) refers to a combination of treatments including cognitive therapy, stimulus control therapy, and sleep restriction therapy with or without relaxation therapy (Schutte-Rodin, Broch, Buysse, Dorsey, & Sateia, 2008). CBT-I is one of the most widely studied treatments for insomnia with a number of studies demonstrating treatment efficacy (for a review of the literature see Buysse, 2013). The effects of CBT-I are comparable (and possibly superior) to those of hypnotic medications over the short term and tend to have more durable effects, even after treatment discontinuation (Mitchell, Gehrman, Perlis, & Umscheid, 2012; Morin et al., 1999; Okajima, Komada, & Inoue, 2011). CBT-I is a treatment typically delivered in weekly sessions over six to ten weeks, requiring a trained practitioner (Troxel & Buysse, 2013). That is, it is not a treatment able to be administered by the general practitioner during a consultation, and therefore requires referral to a trained nurse or therapist. Although CBT-I can be delivered effectively in the primary care setting (Espie, Inglis, Tessier, & Harvey, 2001; Espie et al., 2007), a lack of accessibility and affordability may have limited the widespread use of CBT-I in primary care (Edinger, 2009; Espie, 2009). In response to this, briefer versions of CBT-I, which focus on the components of CBT-I that appear to have the largest effects on treatment outcome (sleep restriction and stimulus control therapy) have been investigated and have shown promising results

(Buysse et al., 2011; Edinger & Sampson, 2003; Morin, Culbert, & Schwartz, 1994). These brief behavioural treatments are discussed further in Section 2.2.3.

Table 2-3: Cognitive Behavioural Treatments for Insomnia

| Treatment (*)                                   | Description   | Underlying theory  |
|---|---|--|
| <b>Stimulus control (Standard)</b>              | Instructions designed to re-establish the association of the bed/bedroom with sleep: only go to bed when sleepy, use the bed/bedroom only for sleep/intimacy, arise at the same time each morning, no napping, and get out of bed if no sleep within 20 minutes and only return when drowsy – repeat as necessary (Bootzin et al., 1991; Schutte-Rodin et al., 2008). | Aims to strengthen the bed as a cue for sleep, rather than wakefulness and frustration. Aims to reduce sleep-interfering activities such as using the bedroom for watching television where the bedroom can become a cue for arousal (Bootzin et al., 1991).   |
| <b>Relaxation training (Standard)</b>           | Procedures designed to reduce the somatic and/or cognitive arousal that can interfere with sleep. For example, progressive muscle relaxation (Schutte-Rodin et al., 2008).  | Reduced arousal facilitates sleep onset.   |
| <b>Cognitive behavioural therapy (Standard)</b> | Multi-component treatment package combining cognitive and behavioural techniques.   |  |
| <b>Sleep restriction (Guideline)</b>            | Initially limits the time in bed to total sleep time (various modifications exist that do not restrict so severely). As sleep continuity improves, time in bed is gradually increased to a point where there is sufficient sleep to feel rested during the day, but sleep continuity is maintained. (Schutte-Rodin et al., 2008; Spielman, Saskin, et al., 1987).     | Excessive time spent in bed perpetuates insomnia. By limiting time in bed, the homeostatic sleep drive is strengthened, the circadian synchrony is restored, the bed becomes a discriminative stimuli for sleep, and hyperarousal is counteracted by partial sleep deprivation (sleepiness) (Spielman, Yang, & Glovinsky, 2011). |

Table 2-3: Cognitive Behavioural Treatments For Insomnia - Continued

| Treatment (*)   | Description  | Underlying theory  |
|---|--|--|
| <b>Paradoxical intention</b><br>(Guideline)                               | A specific cognitive therapy designed to try and shift the focus away from trying to fall asleep by several techniques such as instructions to: try to stay awake, lie comfortably in bed with the lights off but try to keep your eyes open, and give up any effort to try to fall asleep (Morin & Espie, 2003) | Trying to fall asleep increases cognitive arousal (Espie et al., 2006). By trying to stay awake, the patient is giving up trying to fall asleep (thereby increasing the possibility of falling asleep) (Ascher & Efran, 1978). |
| <b>Multi-component therapy (without cognitive therapy)</b><br>(Guideline) | Combination of behavioural techniques. For example:<br>(1) Stimulus control therapy, sleep restriction and sleep hygiene education (Schutte-Rodin et al., 2008)<br>(2) Sleep restriction and stimulus control therapy (Buysse et al., 2011).   |  |
| Sleep hygiene<br>(Insufficient evidence)                                  | Instructions promoting behaviours that assist sleep and discouraging those that interfere with sleep (Hauri, 1991). For example: avoid caffeine in the evening, avoid alcohol, exercise, regularise the bedtime, do not try to sleep, and keep the bedroom dark and quiet.                                       | Eliminating sleep disrupting behaviours and optimising conditions for sleep will assist sleep (Stepanski & Wyatt, 2003).   |
| Cognitive therapy<br>(Insufficient evidence)                              | Psychological methods aimed at changing dysfunctional beliefs and attitudes about sleep (Morin, Bootzin, et al., 2006).  | Negative cognitions lead to arousal and insomnia (Harvey, 2002; Morin, 1993).  |

*Note.* Treatments in bold represent those that meet criteria for empirically-supported psychological treatments for insomnia (Morin, Bootzin, et al., 2006).

\*American Association of Sleep Medicine (AASM) levels of recommendation (Morgenthaler et al., 2006): Standard: a generally accepted patient-care strategy which reflects a high degree of clinical certainty (such as using randomised, well-designed trials); Guideline: a patient-care strategy which reflects a moderate degree of clinical certainty (some poorer-quality evidence than “Standard”); Option: a patient-care strategy which reflects uncertain clinical use (inconclusive or conflicting evidence)

### **2.2.2 Pharmacological treatment**

Pharmacological treatment for insomnia includes both approved hypnotic agents and medications that are not specifically approved for use in insomnia such as antihistamines, tricyclic antidepressants, anxiolytic benzodiazepines, sedating antidepressants, sedating antipsychotics, and anticonvulsants (Buysse, 2013). The hypnotic agents available and approved by the New Zealand Medicines and Medical Devices Safety Authority (MedSafe) are the benzodiazepine receptor agonists (zopiclone, temazepam, lorazepam, triazolam), and the antihistamine diphenhydramine. Benzodiazepine receptor agonists have well-established short-term efficacy in the treatment of insomnia (Krystal, 2009). Studies have also supported the efficacy of nightly or intermittent administration for up to six months (Krystal, Erman, Zammit, Soubrane, & Roth, 2008; Walsh et al., 2007) and up to 12 months in open-label studies (Ancoli-Israel et al., 2005; Thomas Roth, Walsh, Krystal, Wessel, & Roehrs, 2005).

Despite evidence for efficacy, pharmacological treatment for insomnia is associated with important potential adverse effects. Sleeping medications (benzodiazepines or “z-drugs” such as zopiclone) are associated with issues of tolerance, dependence, and withdrawal syndrome and rebound insomnia on cessation (Buysse, 2013; National Institute for Clinical Excellence, 2004; New Zealand Medicines and Medical Devices Safety Authority, 2005, 2007). In rare cases, they can be associated with unusual sleep behaviours (such as “sleep driving” or making phone calls with amnesia for the events) - especially if taken with alcohol (New Zealand Medicines and Medical Devices Safety Authority, 2007). There is also the risk of abuse – hypnotics can enhance the “high” from other drugs and are not uncommonly found to be used in overdose attempts (National Institute for Clinical Excellence, 2004). Further issues include medication interactions, issues of driving under the influence of psychotropics (especially with medications with longer half-lives), and the additional risks that may be involved in prescribing to the elderly (falls, cognitive impairment, and fatigue (Glass, Lanctot, Herrmann, Sproule, & Busto, 2005)) and to those who may have undiagnosed obstructive sleep apnoea (increasing rates of nocturnal hypoxaemia) (New Zealand Medicines and Medical Devices Safety Authority, 2005).

A meta-analysis of efficacy and adverse effects of benzodiazepine receptor agonists in older adults concluded that the risk of adverse effects outweighed the small magnitude of benefits (Glass et al., 2005). When CBT-I and pharmacotherapy were compared directly in a randomised controlled trial in older adults, CBT-I was the superior treatment for both short and long term outcomes (Sivertsen et al., 2006). However, recent research investigating treatment regimens using cognitive behavioural therapy singly, or combined with pharmacotherapy, has demonstrated a potential added benefit for the combination of CBT-I and pharmacotherapy in the acute stage, but with discontinuation of



pharmacotherapy during the maintenance phase of CBT-I treatment for achieving the best long term outcomes (Morin, Vallieres, et al., 2009).

Despite the reservations associated with the use of hypnotic medications, and the long term benefits that may be achieved with non-pharmacological treatments, pharmacologic treatments are currently the most common approach to managing insomnia in the primary care setting (Siriwardena et al., 2009; Terzano, Cirignotta, Mondini, Ferini-Strambi, & Parrino, 2006). This is despite research suggesting patients typically prefer non-pharmacological treatment options over hypnotics (Morin, Gaulier, Barry, & Kowatch, 1992; Vincent & Lionberg, 2001). Therefore, continued investigation into acceptable, effective treatments that are practical for the primary care setting is warranted.

### **2.2.3 Sleep restriction**

*Sleep cannot be produced by a force of will. All we can do is to position ourselves to let it overtake us, like a surfer waiting for a wave (Spielman & Glovinsky, 1991, p. 2).*

#### **Background**

Sleep restriction therapy (SRT) was first described by Spielman and colleagues in the 1980's (Spielman, Caruso, et al., 1987; Spielman, Saskin, & Thorpy, 1983; Spielman, Saskin, et al., 1987). It is a behavioural treatment based on the theory that excessive time spent in bed leads to fragmented, poorer quality sleep (Spielman, 1986). The insomnia is subsequently perpetuated as the sufferer spends a longer time in bed in following nights, hoping to increase their opportunity to achieve more sleep. However, longer periods spent in bed actually lead to more time spent awake in bed, continued poor quality fragmented sleep, and a perpetuated cycle of chronic insomnia (Spielman, Caruso, et al., 1987; Spielman, Saskin, et al., 1987). Poor quality sleep then often leads to increased variability in bed times and wake up times. For example, "sleeping in" after a poor night's sleep, leading to a later time in the evening that one is ready to fall asleep. The consequence of these erratic sleep patterns can then be dyssynchrony with circadian rhythms for sleep and trying to sleep at a time when the biological clock is not ready to promote sleep (Strogatz, Kronauer, & Czeisler, 1987a). Concern over deteriorating sleep can lead to cognitive and physiological arousal, which further perpetuates insomnia (Spielman, Caruso, et al., 1987; Spielman, Yang, & Glovinsky, 2010) (Section 2.1.3).

Sleep restriction has become a widely used treatment for insomnia (Stepanski, 2003). It was rated as an effective and recommended treatment of chronic insomnia in the 2006 American Academy of Sleep Medicine (AASM) recommendation paper both as a single therapy and when part of multicomponent

therapy (Morgenthaler et al., 2006). The recommendation for sleep restriction as a single therapy was based upon two studies using community-dwelling older adults (L. Friedman et al., 2000; Lichstein et al., 2001). Further discussion of these studies can be found in Section 2.3. As part of multicomponent treatments assessed for the AASM recommendation paper sleep restriction was combined with both stimulus control therapy (Waters et al., 2003), and stimulus control and sleep hygiene education (Edinger & Sampson, 2003). Sleep restriction has also frequently been incorporated into cognitive behavioural therapy packages of insomnia treatment (Irwin et al., 2006; Morin et al., 1994; Murtagh & Greenwood, 1995; Wang, Wang, & Tsai, 2005).

### **Theoretical rationale**

Sleep restriction therapy systematically reduces the time spent in bed with the aim of prescribing a “time in bed” allowance that closely matches the average time actually spent sleeping each night (Spielman et al., 1983). This involves ascertaining a current average sleep duration (usually from sleep diaries), and setting a time of getting into bed, and waking up and getting out of bed that corresponds to the average sleep duration. The reduced “time in bed” initially causes a mild sleep deprivation, which increases homeostatic sleep drive (as those with insomnia frequently underestimate total sleep time) (Coates et al., 1982; Spielman, Caruso, et al., 1987). Increased homeostatic sleep drive leads to an increased readiness to sleep at bedtime, increased ease of falling asleep, and a deeper, more consolidated overnight sleep period (in contrast to a light, fragmented sleep) (Mullaney, Johnson, Naitoh, Friedmann, & Globus, 1977; Spielman et al., 2011; Webb, Agnew, & H, 1974; Webb & Agnew, 1965). The experience of falling asleep easily at night serves to strengthen the bed and bedroom as discriminative stimuli for sleep, which reinforces the improved sleep patterns. This also reduces the anxiety about sleep, which can have an alerting effect (Spielman, Caruso, et al., 1987). Figure 2-5 illustrates how erratic sleep in insomnia may be improved by sleep restriction therapy. Table 2-4 describes the mechanism of action of sleep restriction therapy for improving sleep. Table 2-5 describes the basic procedure of implementing sleep restriction therapy.

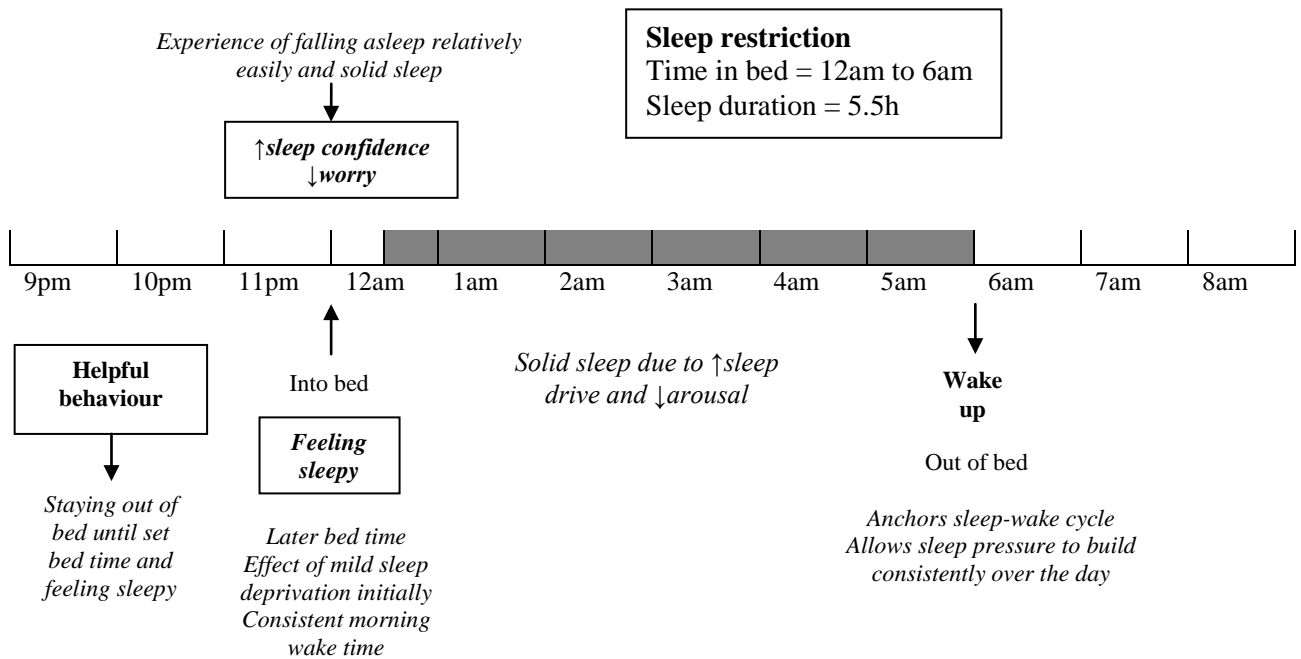
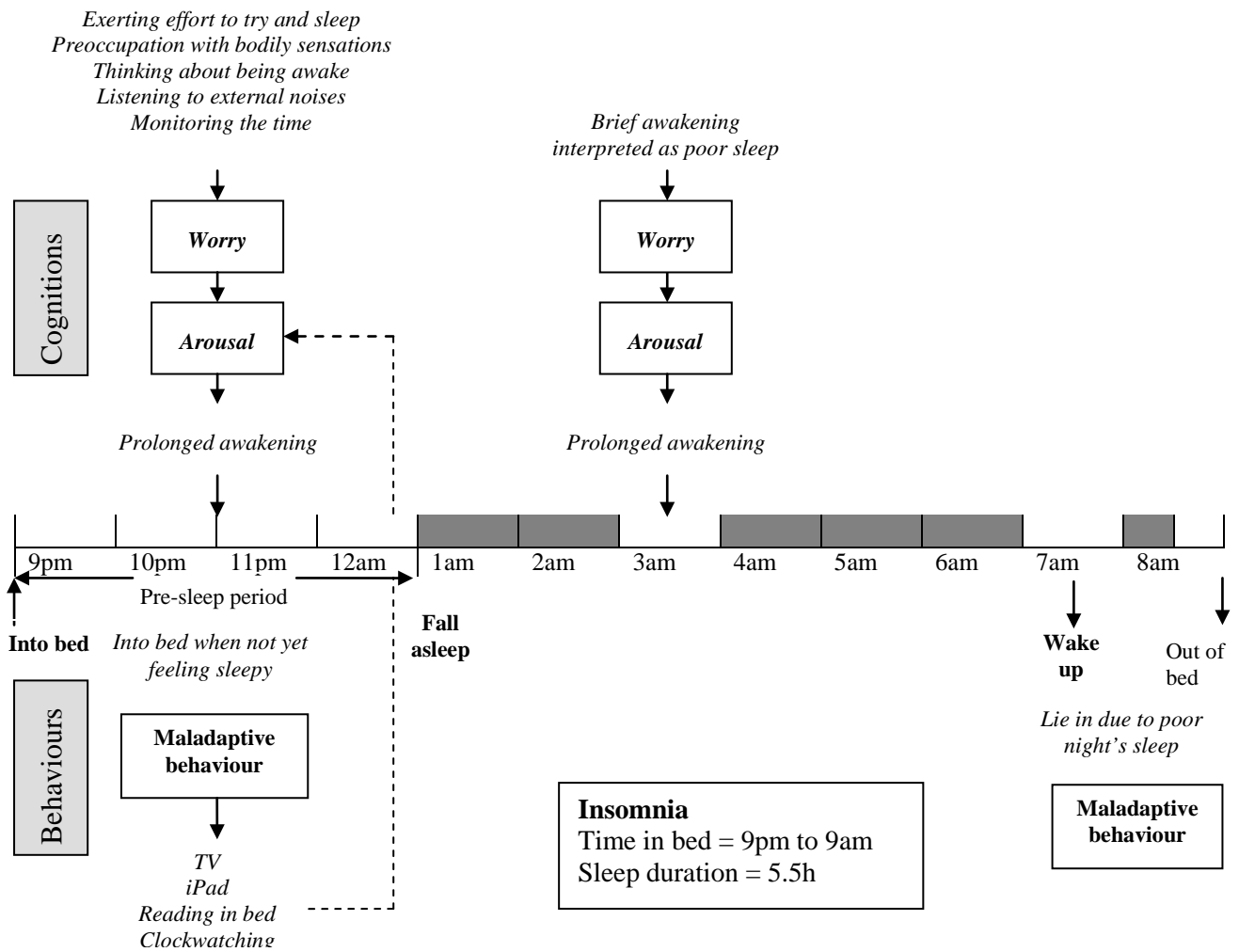


Figure 2-5: Schematic representation of the sleep patterns in insomnia (top) and following a sleep restriction protocol (bottom)

Table 2-4: The Mechanism of Action of Sleep Restriction for Chronic Insomnia

| Process                 | Effect of sleep restriction  | Outcome   |
|-------------------------|--|---|
| Homeostatic sleep drive | Setting a time in bed allowance leads to spending less time in bed and usually, a later bedtime. This may cause a partial sleep deprivation leading to an increase in homeostatic sleep drive (Webb et al., 1974; Webb & Agnew, 1965). Restricting sleep to a period with set limits (bed time and rising time) leads to a consolidated sleep, which tends to be deeper (Spielman et al., 2011; Webb et al., 1974).  | Increased readiness to sleep at bed time (feeling sleepy).<br>Longer periods of sleep, less overnight awakening, deeper sleep.  |
| Arousal                 | The daytime fatigue or sleepiness experienced in the early stages of sleep restriction therapy due to partial sleep deprivation may dampen or counteract chronic hyperarousal (Monroe, 1967; Spielman et al., 2011). The restricted bed time period leads to less time spent lying awake in bed thinking and worrying (Spielman, Caruso, et al., 1987). Bed time instructions to follow may reduce the attention and effort directed towards trying to sleep (Espie et al., 2006; Harvey, 2002). | Increased readiness to sleep at bed time.<br>Less bed time anxiety, therefore less prolonged awakenings.<br>Not having to think about what time to go to bed may lead to eventual disengagement with the worry of bed time (Espie, 2002). |
| Circadian rhythm        | Stable bed time routine leads to enhanced or restored circadian rhythmicity (Spielman et al., 2011). Consistently timed morning awakening and exposure to cues such as morning light help to keep sleep synchronised with circadian rhythms (Spielman et al., 2010). Setting a later bed time helps to avoid the evening “wake maintenance zone” which occurs around 9 to 10pm in those whose habitual sleeping time is between 11pm and 7am (Strogatz et al., 1987a).                           | Promotes wakefulness during the day and an effortless transition to sleep at bed time.<br>Sleep and wakeful phases have a more reliable timing (Spielman et al., 2011). A later bed time means falling asleep faster.                     |

Table 2-5: Procedure for Implementing Sleep Restriction Therapy

| Instruction  | Explanation  |
|--|--|
| Estimate time spent in bed and time spent asleep           | <p>Average nightly total sleep duration gives a starting point for the prescription of a bed time allowance.</p> <p>Depending on the method used (rapid or gradual), the bed time allowance may be equal to the estimated average sleep duration (with a minimum of five hours), or the estimated average sleep duration plus a percentage of the excess awake time spent in bed.</p>  |
| Prescribe time in bed allowance, bed time and wake up time | <p>Bed time and wake up (out of bed) time are negotiated with the patient and written down. The agreed regimen is kept constant for a period of time, for example, two weeks.</p>  |
| Review after two weeks                                     | <p>Progress is discussed and adjustments made either using sleep diaries or recall. Questions may include:</p> <p>“How is your sleep?” “How many hours of sleep are you getting each night, on average?”</p> <p>“How long, on average, does it take you to fall asleep?”</p> <p>“How long, on average, are you awake overnight after initially falling asleep?”</p> <p>“How much earlier than your wake up time are you finally waking?”</p> <p>“Are you feeling sleepy, sleep deprived, or impaired during the day because of poor sleep?”</p>  |
| Adjustments<br>(Spielman et al., 2011)                     | <p>Time in bed allowance is reduced if there is unsatisfactory excess time awake (for example, taking too long to fall asleep, or being awake for too long over night) or sleep efficiency <math>\leq 85\%</math> (<math>\leq 80\%</math> in older adults).</p> <p>Time in bed allowance is lengthened if there is daytime sleepiness or impairment or sleep efficiency <math>\geq 90\%</math> (<math>\geq 85\%</math> in older adults).</p> <p>Time in bed allowance is unchanged if sleep is satisfactory or sleep efficiency between 85 and <math>&lt; 90\%</math> (80 to <math>&lt; 85\%</math> in older individuals).</p> |
| Further review and adjustment as required                  | <p>Once satisfactory, consolidated sleep is obtained there is the opportunity to lengthen the time in bed allowance (as long as satisfactory, consolidated sleep is maintained).</p>   |

### **Sleep restriction as a single component treatment for insomnia**

As previously mentioned, the American Academy of Sleep Medicine (AASM) has recommended sleep restriction as an effective single treatment for chronic insomnia. However, this recommendation was made on the basis of older adult participants recruited from the community (L. Friedman et al., 2000; Lichstein et al., 2001). Therefore, the efficacy of sleep restriction as a single component treatment for insomnia both in younger (as well as older) adults, and in the primary care setting has yet to be established.

Brief behavioural treatment packages combining sleep restriction and stimulus control have shown encouraging efficacy in the primary care setting (Buysse et al., 2011; Edinger & Sampson, 2003). The study by Edinger et al. (2003) was a small trial ( $n = 20$ ), in which the participants were recruited from a Department of Veterans' Affairs Medical Centre. Both older and younger adults were included and the participants were predominantly male (90%). In Buysse et al. (2011), some of the participants in the study were recruited from a primary care clinic with the remainder from the community. However, the study was limited to older adults, and included those with co-morbid conditions, rather than just those with primary insomnia. Even so, the treatment was designed for implementation in the primary care setting, although not designed to be delivered by the general practitioner during the consultation. It also required two extended appointments (45 to 60 minutes and 30 minutes) and two follow up phone calls (Buysse et al., 2011). It is unlikely that this intensity of regimen both in time for patient, cost to patient, and cost in terms of practice nurse time is practical for widespread dissemination in general practice. A shorter form of this intervention may be more suitable for the primary care setting.

Therefore, there remains a gap in knowledge in regards to an effective non-pharmacological treatment for chronic primary insomnia in adults that can be delivered during the primary care consultation. A recent study by Epstein, Sidani, Bootzin, and Belyea (2012) directly compared the effectiveness of these multi-component treatments (sleep restriction plus stimulus control) with the single components. The study showed that the multi-component intervention, sleep restriction, and stimulus control were equally efficacious in improving sleep and clinical measures both at post treatment and at one year follow up (Epstein, Sidani, Bootzin, & Belyea, 2012). Whilst published after the start of the current ReFRReSH trial, the Epstein trial lends support to the possibility that a single component treatment has the benefits of a more complicated multi-component regimen. The ReFRReSH trial of this thesis was designed to address the gap in knowledge that exists for an effective, feasible insomnia treatment for primary care. In the ReFRReSH trial, the choice of sleep restriction as a single component treatment for insomnia was based on experience in clinical practice and the encouraging results of the pilot study looking at sleep restriction as a single component treatment for insomnia (Fernando, Arroll, & Falloon, 2013).

## **2.3 Systematic Review of Sleep Restriction for Primary Insomnia**

### **2.3.1 Introduction**

Non-pharmacological treatments are effective for treating insomnia, however this recommendation is based mainly on multi-component treatments such as cognitive behavioural therapy for insomnia (Morgenthaler et al., 2006). Cognitive behavioural therapy for insomnia usually requires referral to an experienced practitioner and multiple weekly sessions. Therefore, acceptability, accessibility, and affordability can be significant issues (Espie, 2009). An important gap in current knowledge is the effectiveness of sleep restriction alone rather than as a component of a package of treatment such as cognitive behavioural therapy for insomnia. Single-component therapy may be a treatment option that could be feasible for use in the primary care setting. This section describes a systematic review of the published evidence on the effectiveness of sleep restriction compared to control for the treatment of primary insomnia using randomised controlled trial study design. The primary outcomes of interest were sleep quality and efficiency.

### **2.3.2 Methods**

#### **Protocol and registration**

This systematic review was registered prospectively on PROSPERO – the international prospective register of systematic reviews (<http://www.crd.york.ac.uk/PROSPERO, CRD42013005147>). The review question was defined as: “In adults with primary insomnia, is sleep restriction an effective treatment compared to control?”.

#### **Eligibility criteria**

##### ***Participants***

This review was limited to adults with primary insomnia. Adults include those aged 16 years or older. Studies were included if participants were defined as “adults” or “older adults” without specific age parameters. Studies were included if they included those with “primary insomnia” or with “insomnia” (as long as the method demonstrated an effort to exclude other sleep disorders). Studies were excluded if they included participants with sleep disorders other than primary insomnia, who were suffering from comorbid insomnia (secondary insomnia), or who were currently medically unwell or unstable.

##### ***Interventions***

All forms of sleep restriction were included. This included interventions called “sleep scheduling” but which involved only sleep restriction instructions (rather than a combination of methods). Also included were modifications of traditional sleep restriction such as sleep compression (where the

restricting of the time allowed in bed is done progressively rather than abruptly). The procedure of sleep restriction was as defined by the researcher relating to matching the time spent in bed with sleep duration.

**Outcomes**

Outcomes are shown in Table 2-6. Where possible, the outcomes were divided into short-term (immediately post treatment), medium term (3 to 12 months), and long term (greater than 12 months). Multiple comparisons were assessed in this systematic for two main reasons. Firstly, assessing a variety of sleep and daytimes outcomes helped to reflect the multidimensional nature of insomnia (Morin, 2003). Secondly, there has been very little standardisation of the assessment of outcomes in insomnia research prior to the publication of research recommendations in 2006 (Buysse et al., 2006). Previous Cochrane Collaboration insomnia reviews have used a multiple comparisons of outcome measures (Cheuk, Yeung, Chung, & Wong; Montgomery & Dennis, 2003). The current systematic review and meta-analysis has followed this convention. However, a limitation of this approach is that using multiple outcome measures in the meta-analysis may risk detecting a statistically significant effect where there is no real effect (type I error) (Feise, 2002).

*Table 2-6: Primary and Secondary Outcomes for the Systematic Review of Sleep Restriction for Primary Insomnia*

| <b>Primary</b>   | <b>Secondary</b>  |
|--|---|
| Subjective report of sleep quality e.g. Pittsburgh Sleep Quality Index (Buysse et al., 1989) and Insomnia Severity Index (Bastien, Vallieres, & Morin, 2001) | Sleep onset latency (SOL)<br>Wake after sleep onset (WASO)  |
| Sleep efficiency (total sleep duration/time in bed x 100%).  | Total sleep time (TST)<br>Daytime functioning related to sleepiness (e.g. Epworth Sleepiness Score (Johns, 1991)) and fatigue |
|  | Quality of life   |
|  | Frequency of adverse effects  |



### ***Study design***

This review was limited to randomised controlled trials, in any language, that allocated participants to sleep restriction (bedtime restriction, sleep compression) or a control condition (wait list, no treatment, usual care, or sleep hygiene if also received by the intervention group).

The randomised controlled trial design was chosen because it represents the “gold standard” trial design to assess the efficacy of interventions and minimises the risk of bias (Altman, 1991; Altman et al., 2001).

### ***Report characteristics***

There was no restriction to the years considered for this review. There were no limits applied to the search in regard to language or publication status.

### ***Information sources***

The following databases were searched for articles in any language and in any time period up until the end of July 2013: MEDLINE (1950 to June 2013), The Cochrane Central Register of Controlled Trials (The Cochrane Library, Issue 6, June 2013), CINAHL Plus (1937 to 2013), EMBASE (1980 to 2013), PubMed (1946 to 2013), and PsychINFO. The last search was performed 21/7/13.

Supplementary methods of finding studies for this review included studying reference lists of articles identified through the database searches and review articles for the non-pharmacological treatment of insomnia.

### ***Search***

Tables 2-7 and 2-8 list the search strategy for the MEDLINE database search. “Behavioural treatment” search terms and “insomnia” search terms were combined with “AND” before using “OR” to combine with the “sleep restriction” search terms. The same search terms were used in the other database searches. No limits were applied to the searches except for limiting the search to “human” in the PubMed search due to the large number of citations found.

*Table 2-7: Insomnia and Behavioural Treatment Search Terms Combined in the MEDLINE Database Search*

| <b>Insomnia search terms</b>   | <b>Behavioural treatment search terms</b>  |
|--|--|
| “Sleep Initiation and Maintenance Disorders”/<br>Insomnia.mp<br>Primary insomnia.mp<br>Sleep Disorders/<br>Sleep difficulty.mp<br>Sleep/<br>Wakefulness/ | Behavior Therapy/<br>Non-drug treatment.mp<br>Non-pharmacological treatment.mp<br>Behaviour modification.mp<br>Behaviour modification.mp<br>Behaviour therapy.mp |

*Note.* The insomnia search terms and Behavioural treatment search terms were combined with “AND” in the Medline database search. The forward slash (/) denotes a MEDLINE Subject Heading term (MeSH). The suffix .mp denotes a multi-purpose search which looks in the Title, Original Title, Abstract, Subject Heading, Name of Substance, and Registry Word fields.

*Table 2-8: Sleep Restriction Search Terms Used in the MEDLINE Database Search*

| <b>Sleep restriction search terms</b> |
|---------------------------------------|
| Sleep restriction.mp                  |
| Bedtime restriction.mp                |
| Bed time restriction.mp               |
| Bed restriction.mp                    |
| Sleep period reduction.mp             |
| Sleep retraining.mp                   |
| Sleep compression.mp                  |
| Sleep consolidation.mp                |
| Sleep scheduling.mp                   |
| Sleep reorganisation.mp               |
| Sleep reorganization.mp               |
| Sleep prescription.mp                 |
| Bed prescription.mp                   |
| Bedtime prescription.mp               |
| Bed time prescription.mp              |

## **Study selection**

All citations produced by the search strategy were screened and duplicates deleted. The abstracts of potential studies identified were reviewed for relevance against the selection criteria. Potential studies were those where there was any indication of insomnia or sleep being investigated and either sleep restriction or a behavioural treatment that could potentially refer to sleep restriction was being investigated. Citations were excluded if they clearly met exclusion criteria (for example, the study population was those with depression, or there was clearly no control or randomised study design used). Full text articles were obtained for abstracts that met inclusion criteria. The full text articles were independently assessed by two reviewers (KF and BA) to determine if they met inclusion criteria using a form designed by the author (KF) (see Appendix A for included studies). Disagreements regarding relevance were resolved by discussion by both the reviewers. If resolution was not possible, a third reviewer (CRE) was available to provide arbitration. There was no blinding regarding the authors, institutions or journal of publication. Excluded studies and reasons for exclusion were documented (Appendix B). Critical appraisal was performed on the included studies.

## **Data collection process**

Information was extracted from the full text articles independently by each of the two reviewers (KF and BA) using a data extraction form designed by the author in accordance with recommendations from the Cochrane Collaboration (Higgins, Altman, & Stern, 2011) (Appendices C and D).

## **Data items**

Quality assessment was undertaken in two steps. Firstly, studies were assessed based on the recommendations from the Cochrane Collaboration (Higgins, Altman, & Stern, 2011). Secondly, the quality of each study was appraised using the “GATE method” validity criteria which were designed specifically for appraising the quality of randomised controlled trials (Jackson et al., 2006). The GATE method validity criteria make the mnemonic “RAAMbo”:

- **Representative:** Are the participants representative of the eligible population?
- **Allocation:** How were participants allocated to intervention and comparison groups? How was randomisation performed? Was there adequate generation of allocation sequences (adequate if sequences are suitable to prevent selection bias such as the use of computerised random number generation) (Juni, Altman, & Egger, 2001)? Was there adequate concealment of allocation sequences (adequate if the patients and those enrolling the patients cannot foresee the next assignment) (Juni et al., 2001)? Was there balance in the baseline characteristics of the intervention and comparison groups suggesting adequate randomisation?

- Accounted: All participants need to be accounted for at the end of the study. The overall number of participants should be equal to those in the intervention and comparison groups, which should be equal to those with and without the specified study outcome (Jackson et al., 2006).
- Measurement: Was the assessment of outcomes *blind* to knowledge of the intervention or comparison group? Was measurement of outcomes *objective* (subjective outcomes have a potential for error in their measurement) (Jackson et al., 2006)?

Two additional criteria were used for quality assessment of statistical analyses:

1. Was the intention-to-treat principle adhered to? This is a strategy whereby participants are analysed according to the group they were originally assigned to, regardless of the treatment they actually received, or any drop outs (Hollis & Campbell, 1999).
2. Was there adjustment for any potential confounding variables? Confounding is defined as “a difference between treatment groups in the characteristics that influence the association between the treatment and outcome measures”(Sedwick, 2012, p. e7951). Confounding can lead to either underestimation or overestimation of treatment effect, and inaccurate study conclusions. The items considered in the quality assessment of studies are summarised in Table 2-9.

Table 2-9: Quality Assessment of Studies in the Systematic Review of Sleep Restriction as a Treatment for Insomnia

| Variable            | Questions to consider  | Variable                     | Questions to consider   |
|---------------------|--|------------------------------|---|
| Methods and setting | Study design, total study duration<br>Sequence generation, allocation sequence, concealment, blinding, other concerns about bias   | Intervention                 | Total number of intervention groups<br>Specific intervention<br>Intervention details (sufficient for replication)             |
| Participants        | Total number, setting, age, sex<br>Diagnostic criteria, country<br>Co-morbidity, socio-demographics, ethnicity<br>Date of study  | Outcome and time             | Outcomes and time points (collected? reported?)<br>For each outcome of interest:<br>Outcome definition<br>Unit of measurement |
| Results             | Number of participants allocated to each intervention group<br>For each outcome of interest:<br>sample size, missing participants<br>Summary data for each intervention group<br>Estimate of effect with confidence interval; P value                    | Intention-to-treat analysis? | Was analysis performed in accordance with the principle of intention-to-treat?  |
| RAAMbo              | <i>Representative</i> participant population?<br><i>Allocation</i> (randomisation and allocation concealment adequate)?<br><i>Accounted</i> (are all participants accounted for in groups and outcomes)?<br><i>Measurement – blind and/or objective?</i> | Confounding                  | Was there any adjustment for potential confounding?   |

Note. Quality assessment based on Jackson et al. (2006) and Higgins, Altman, and Stern (2011).

## **Risk of bias in individual studies**

In accordance with the recommendations of the PRISMA statement for reporting systematic reviews, methodological components (rather than scales or checklists) were used to assess the overall risk of bias in the included studies (Liberati et al., 2009). Risk of bias was assessed using the Cochrane Collaboration's tool for assessing risk of bias (Higgins, Altman, & Stern, 2011). Assessing for risk of bias is an important step in critical appraisal of studies as limiting bias is important to reduce the risk of making inaccurate conclusions about the treatment effects (Gluud, 2006). As yet, there is no gold-standard method for the assessment of risk of bias in randomised controlled trials (Katrak, Bialocerkowski, Massy-Westropp, Kumar, & Grimmer, 2004). There are a number of scales that have been developed to assist the assessment of the risk of bias in studies (Moher et al., 1995). However, the use of scales for assessing the risk of bias have been criticised by some due to the lack of empirical support for their use (Emerson, Burdick, Hoaglin, Mosteller, & Chalmers, 1990), being unreliable assessments of validity (Juni, Witschi, Bloch, & Egger, 1999), and the limited transparency they provide for readers of the review (Higgins, Altman, & Stern, 2011). The Cochrane Collaboration's tool for assessing the risk of bias was developed in an effort to address some of the deficiencies identified in the existing quality assessment tools (Higgins, Altman, Gotzsche, et al., 2011). It is a domain-based evaluation where seven domains are categorised, with support for judgement and justifying comment, as at "low risk" of bias, "high risk" of bias or "unclear risk" of bias (Higgins, Altman, & Stern, 2011). An overall judgement is then made on the basis of the individual domain judgements. The domains evaluated are listed below:

- Random sequence generation
- Allocation concealment
- Blinding of participants and personnel
- Blinding of outcome assessment
- Incomplete outcome data
- Selective reporting
- Other sources of bias

## **Summary measures**

Meta-analysis was performed when more than one study reported a comparable outcome measure. The mean difference in measurement or score in the sleep restriction group compared to the control group was entered into Review Manager software (version 5.2) to produce a meta-analysis with summary effect score and 95% confidence interval (Review Manager (Version 5.2)). Forest plots were then able to be generated. Combining mean treatment effects when scales were different but comparable was made possible by combining the standard mean difference. This required transformation to standardised

values by dividing the mean by the sample standard deviation in each study (Liberati et al., 2009) (Montgomery & Dennis, 2003).

If attrition rates were greater than 30% then the studies were not included in analysis as the potential for bias was considered unacceptably high (Montgomery & Dennis, 2003).

### **Risk of bias across studies**

Statistical heterogeneity was assessed using the  $I^2$  test for inconsistency (Higgins, Thompson, Deeks, & Altman, 2003). If studies were heterogeneous, a random-effects model was used for statistical analysis. If there was no significant heterogeneity, a fixed effects model was used.

The possibility of a publication bias was to be assessed by visually evaluating a funnel plot of the trial mean differences for asymmetry (Liberati et al., 2009). In funnel plots asymmetry can result from the non-publication of small trials with negative results, but also from differences in trial quality of true study heterogeneity (Egger, Davey Smith, Schneider, & Minder, 1997; Sterne et al., 2011). However, due to the small number of trials, this was not possible.

### **Additional analyses**

A subgroup analysis was planned, where only studies meeting all the criteria (in addition to being randomised controlled trial in adults with insomnia) listed in the abstract review table were included in analysis (Appendix A). The criteria were:

1. Insomnia diagnosed using standard criteria such as DSM-IV (American Psychiatric Association, 2000) or International Classification of Sleep Disorders (American Sleep Disorders Association, 2005) criteria); and standardised measures (for example using the Pittsburgh Sleep Quality Index (Buysse et al., 1989)), objective measures (for example polysomnography or actigraphy), or by sleep diaries,
2. Exclusion of those with other sleep disorder or comorbid/secondary insomnia, and
3. The use of validated outcome measure (e.g. PSQI), objective measure (e.g. PSG or actigraphy), or sleep diaries.

However, subgroup analysis was not performed due to the small number of included studies.

### **2.3.3 Results**

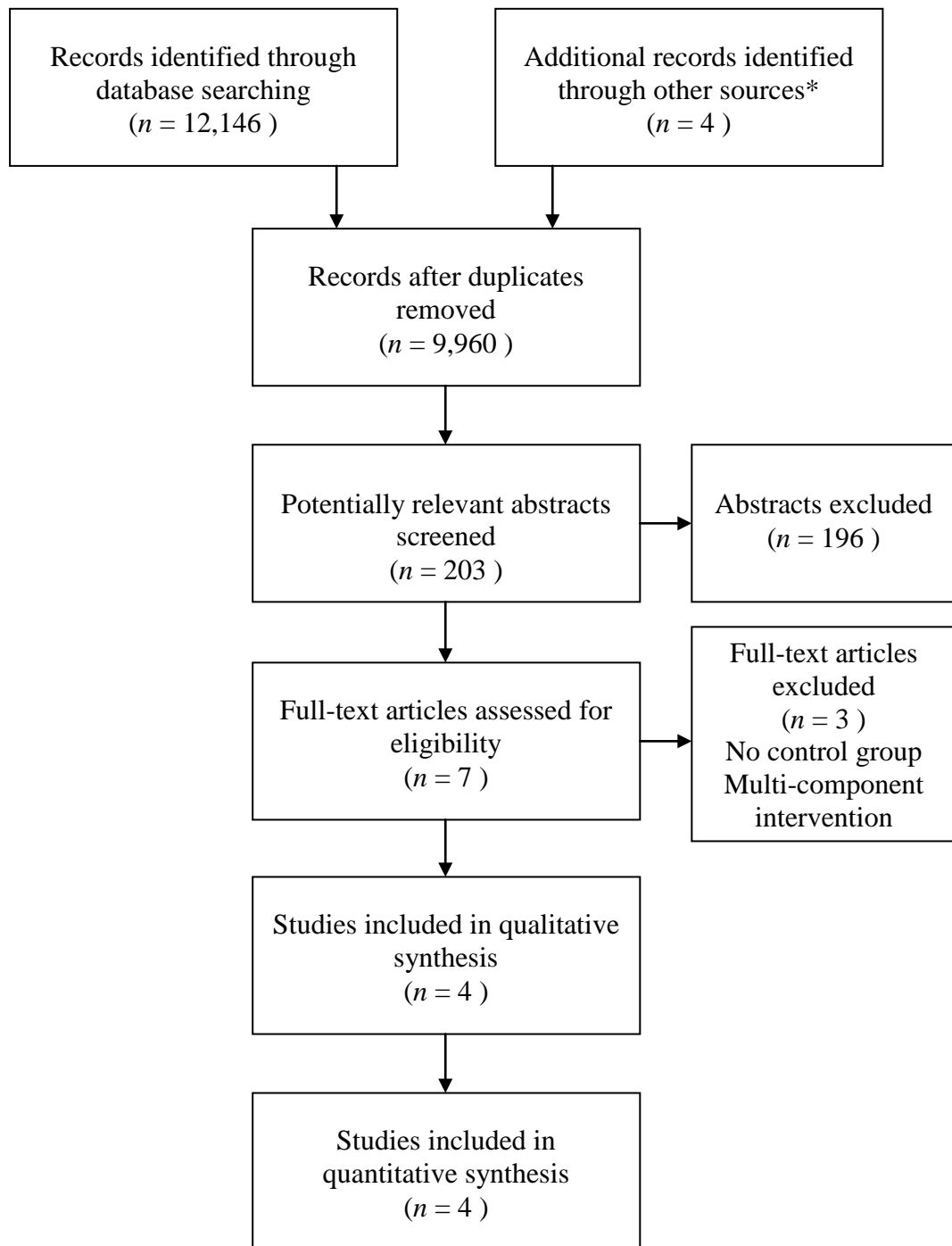
#### **Study selection**

The results of the systematic literature search are summarised in the PRISMA flow diagram in Figure 2-6. The search of MEDLINE, The Cochrane Central Register of Controlled, CINAHL Plus, EMBASE, PubMed, and PsychINFO provided a total of 12,146 citations. After duplicates were removed, 9,960 citations remained. Of these, 9,757 studies were excluded because it appeared the papers clearly did not meet the criteria. Abstracts were reviewed of the remaining 203 studies. A further 196 studies were excluded as they did not meet the exclusion criteria. Common reasons for exclusion were studies in children or using cognitive behavioural therapy multi-component treatments. The full text of the remaining seven studies were reviewed. Two studies were excluded as they did not have control groups (Kyle, Morgan, Spiegelhalder, & Espie, 2011; Spielman, Saskin, et al., 1987). One study was excluded as the sleep restriction intervention was combined with sleep hygiene and sleep education, therefore it was considered to be a multi-component intervention (Epstein et al., 2012). The excluded studies are shown in Appendix B.

Four studies met the inclusion criteria and were included in the systematic review (Fernando et al., 2013; L. Friedman et al., 2000; Lichstein et al., 2001; Riedel, Lichstein, & Dwyer, 1995). Three of the four studies used outcome measures that allowed quantitative synthesis or meta-analyses. No additional studies were identified by checking the reference lists of 11 meta-analyses of non-pharmacological treatments for insomnia. No unpublished studies were obtained.

The included studies appraised according to the Cochrane Collaboration recommendations and “RAAMbo” were entered into the data extraction tables (Appendix D).





\*Review articles of non-pharmacological treatments for insomnia (Cheng & Dizon, 2012; Irwin et al., 2006; Montgomery & Dennis, 2003; Morin et al., 1999; Morin et al., 1994; Murtagh & Greenwood, 1995; Okajima et al., 2011; Pallesen, Nordhus, & Kvale, 1998; M. T. Smith et al., 2002; van Straten & Cuijpers, 2009; Wang et al., 2005)

Figure 2-6: Flow diagram of study selection for the systematic review of sleep restriction for treating primary insomnia

## **Study characteristics**

### ***Methods***

The four studies included in this review were published between 1995 and 2013 (Fernando et al., 2013; L. Friedman et al., 2000; Lichstein et al., 2001; Riedel et al., 1995). Three of the trials were conducted in the United States (Riedel 1995; Friedman 2000; Lichstein 2001) and one in New Zealand (Fernando 2013). At least three of the trials recruited participants from media advertisements (Riedel 1995; Lichstein 2001; Fernando 2013). The duration of the intervention was three weeks (Riedel 1995), four weeks (Friedman 2000), and six weeks (Lichstein 2001; Fernando 2013). While all the trials assessed outcomes immediately after the intervention (“post-treatment”), three of the four studies also assessed outcomes at a later “follow up” time point. These follow up outcome assessments were performed at two months (Riedel 1995), three months (Friedman 2000), and one year post-treatment (Lichstein 2001).

### ***Participants***

The trials were relatively small, with the included studies involving a total of 298 participants. Three of the studies involved only older adults aged 55 years or older (Riedel 1995; Friedman 2000; Lichstein). One study included adults aged 16 years or older (Fernando 2013). All studies had more female participants than male participants (overall 67% female). In the two studies that reported ethnicity data, the majority of participants reported a white or European ethnicity (Lichstein 2001; Fernando 2013). For all studies the participants were required to discontinue sleeping medication at least three weeks before entering the study and to abstain from use for the duration of the study. Two of the studies screened participants for obstructive sleep apnoea and periodic limb movements of sleep using overnight monitoring (Friedman 2000; Lichstein 2001). All studies screened participants for potential causes of secondary or comorbid insomnia using interviews or self-report questionnaires.

The insomnia diagnostic criteria used by Riedel et al. (1995) were: self-perception of insomnia, symptoms of insomnia at least three times per week for at least a year. The symptoms of insomnia were: sleep latencies > 30 minutes, frequent or lengthy awakenings during the night, or an inability to return to sleep after early morning awakening (Riedel et al., 1995). All participants met the *Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R)* quantitative requirements of insomnia at least three times per week, for at least one month (American Psychiatric Association, 1987). Friedman et al. (2000) required participants to meet sleep diary eligibility criteria based on mean values on a two week recording: sleep efficiency < 80%, sleep onset latency > 30 minutes, or total sleep time < 6 hours, or >30 minutes of wake time after sleep onset on 5 nights during the two weeks. In addition, each participant received an *International Classification of Sleep Disorders* diagnosis (American Sleep Disorders Association, 1990). Lichstein et al. (2001) required a difficulty initiating or maintaining sleep

for at least six months, a complaint of daytime impairment, and an indication of learned sleep preventing associations. This diagnostic criteria corresponds to the *International Classification of Sleep Disorders* classification of psychophysiological insomnia (American Sleep Disorders Association, 1990). In addition, sleep onset latency > 30 minutes or >30 minutes of wake time after sleep onset occurring on average at least three times per week were required for inclusion. Fernando et al. (2013) defined primary insomnia according to the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR)* diagnostic criteria which required difficulty with sleep initiation or maintenance occurring at least three nights per week, for at least one month, with no other identified cause of the insomnia (American Psychiatric Association, 2000).

### ***Interventions***

All of the included trials varied in regards to the specific sleep restriction method and control condition used. The comparison of these methods is presented in Table 2-10. In addition, one study permitted a daily 30 minute nap (no later than 2pm) if there was participant resistance to the prescribed sleep compression schedule (Lichstein 2001).

Table 2-10: Comparison of Intervention and Control Instructions for the Included Studies

| <b>Study</b>   | <b>Intervention</b>   | <b>Control</b>   |
|----------------|---|--|
| Riedel 1995    | Sleep compression plus sleep education video<br>Reduce excess time in bed by 50% at baseline visit. At second visit reduce by 25% of the baseline excess. At third visit reduce by 25% of baseline excess.  | Sleep education video  |
| Friedman 2000  | Sleep restriction plus sleep hygiene (which included stimulus control)<br>Time in bed initially restricted to mean total sleep time over 14 days. Weekly incremental increases in time in bed according to a fixed algorithm based on initial total sleep time. All subjects reach 7 hours in bed by the end of the 4 <sup>th</sup> week. | Sleep hygiene (which included stimulus control)  |
| Lichstein 2001 | Sleep compression<br>Average total sleep time and time in bed was determined by sleep diaries. The difference was divided by 5, and allotted time in bed compressed by this amount weekly. Revised sleep schedule given each week. Time in bed increased if sleep efficiency > 90%.   | Placebo desensitisation<br>This involved constructing a temporal hierarchy of 10 bedtime events e.g. having a snack, brushing teeth. |
| Fernando 2013  | Sleep restriction plus sleep hygiene<br>Time in bed restricted to average total sleep time (minimum duration 5 hours). This was set at baseline and maintained for six weeks.   | Sleep hygiene  |

### ***Outcomes***

The study outcomes are presented in Table 2-11. Fernando et al. (2013) were simply asked how well they had been sleeping in the past month in comparison to before the study (“much worse”, “worse”, “same”, “better” or “much better”). This outcome was not a validated scale and was a limitation of the study quality. No study included adverse events or effects as an outcome.

### **Risk of bias within studies**

#### ***Allocation***

Two studies reported methods of adequate randomisation (Friedman 2000, and Fernando 2013). Additional information was gathered for a third study, which also had an adequate method (Lichstein 2001). No information was available for Reidel et al. (1995), which was therefore assigned an “unclear risk” of bias. Three studies were rated “unclear risk” of bias due to a lack of information regarding allocation concealment. Only Fernando et al. (2013) reported concealed allocation (using opaque envelopes) and was therefore allocated a “low risk” rating.

#### ***Blinding***

Although blinding is more difficult in trials of non-pharmacological interventions, a lack of double blinding has been reported to exaggerate treatment effect (Boutron, Tubach, Giraudeau, & Ravaud, 2004; Schulz, Chalmers, Hayes, & Altman, 1995). Two studies had inadequate reporting of blinding and were therefore considered “unclear risk” of bias (Riedel 1995, Lichstein 2001). Two studies (Friedman 2000, Fernando 2013) reported blinding. In the study by Freidman et al. (2000), the participants were assumed to be blinded to the treatments (“at no point was assignment unblinded”, p.19). The therapists were not blinded to the subjects’ treatment assignment, but were blind to subject outcomes. Paper records for polysomnography were blinded so that scoring was carried out without any knowledge of treatment assignment. However, it was not reported whether other outcome assessments were blinded. In the study by Fernando et al. (2013), the participants were unaware as to whether they were in the intervention or control group. The therapists (the investigators) were not blind to the group allocation. However, the outcome assessor was blind to the group allocation of the participants.

#### ***Incomplete outcome data***

Drop-out rates varied from 0 to 17% between studies. Riedel et al. (1995) had no attrition. Fernando et al. (2013) had a 4% attrition rate and used an intention-to-treat analysis with the missing participants being allocated their baseline status. Friedman had a 10% attrition rate with an intention-to-treat analysis also using baseline values carried forward for missing values. The Lichstein et al. (2001) study had an attrition rate of 17%. Despite the higher attrition rate, the trial was 12 months in duration,

compared with the other trials that were of three months or less duration, so a 17% attrition rate would still be considered low.

### ***Other potential sources of bias***

No studies reported adjustment for potential confounders although the Friedman et al. (2000) study reported using a modified Efron procedure to “equate conditions on initial TST [total sleep time] and napping” (p. 19). Lichstein et al. (2001) reported that “participants were stratified on gender, sleep efficiency, and IIS scores based on estimated median splits and randomly assigned ... within strata” (p. 230). Riedel et al. (1995) described partial matching, “towards the end of the study...participants were assigned to conditions to satisfy matching criteria on age and gender” (p. 57).

### **Results of individual studies**

The summary of included studies is shown in Table 2-11. Two studies had multiple comparison groups (Reidel 1995, Friedman 2000). For the purposes of this review, only the sleep restriction intervention and control intervention are compared.

Table 2-11: Summary of Included Studies Evaluating the Efficacy of Sleep Restriction for Primary Insomnia

| Study                   | Participant characteristics   | Intervention and control  | Outcomes   | Follow up                  |
|-------------------------|---|---|--|----------------------------|
| Reidel et al.<br>1995   | Community<br>Age $\geq$ 60 years old<br><i>N</i> = 50<br><i>DSM-III</i> insomnia diagnosis<br>Other sleep disorders excluded using interviews using general health and sleep questionnaires (not named)   | Video (sleep education) plus sleep compression therapy (4 sessions)<br><br>Video alone (2 sessions) | Sleep diary sleep parameters (SOL, TST, TIB, WASO, SE)<br>Stanford Sleepiness Scale <sup>a</sup><br>Sleep satisfaction scale (1-10) <sup>b</sup><br>Sleep knowledge quiz (0-9) | Post treatment<br>2 months |
| Friedman et al.<br>2000 | Community<br>Age $\geq$ 55 years old<br><i>N</i> = 27<br><i>ICSD</i> insomnia diagnosis<br>Other sleep disorders excluded using structured telephone interview, sleep disorders questionnaire, Geriatric Depression Scale, Folstein Mini Mental States Exam, and structured clinical interview for DSM-IV | Sleep restriction plus sleep hygiene ( 6 sessions)<br><br>Sleep hygiene alone (6 sessions)          | Sleep diary and actigraphy sleep parameters (SOL, TST, WASO, SE)<br>Subgroup polysomnography   | Post treatment<br>3 months |

Table 2-11: Summary of Included Studies Evaluating the Efficacy of Sleep Restriction for Primary Insomnia - Continued

| Study                    | Participant characteristics   | Intervention and control  | Outcomes   | Follow up                    |
|--------------------------|---|---|--|------------------------------|
| Lichstein et al.<br>2001 | Community<br>“Older adults” mean age 68 years old<br>(range 59-92 )<br><i>N</i> = 89<br><i>ICSD</i> insomnia diagnosis<br>Other sleep disorder diagnoses excluded<br>using structured interview | Sleep compression (6 sessions)<br><br>Placebo desensitisation                                   | Sleep diary and<br>polysomnography sleep<br>parameters (SOL, TST, WASO,<br>SE, napping)<br>Sleep stages<br>Sleep quality (1-5 scale) <sup>b</sup><br>Insomnia Impact Scale <sup>c</sup><br>Beliefs and Attitudes about<br>Sleep Scale <sup>d</sup><br>Fatigue Severity Scale <sup>e</sup><br>Epworth Sleepiness Scale <sup>f</sup> | Post treatment<br><br>1 year |
| Fernando et al.<br>2013  | Community<br>Adults ≥ 16<br><i>N</i> = 45<br><i>DSM – IV – TR</i> insomnia diagnosis<br>Other sleep disorders excluded using<br>questionnaire and interview                                     | Sleep restriction plus sleep<br>hygiene (2 sessions)<br><br>Sleep hygiene alone (2<br>sessions) | Self-reported sleep<br>improvement: “much better”,<br>“better”, “same”, “worse”,<br>“much worse” <sup>b</sup>  | 6 weeks                      |

*Note.* <sup>a</sup>Stanford Sleepiness Scale (Hoddes, Zarcone, Smythe, Phillips, & Dement, 1973). <sup>b</sup>Not reported as a validated scale. <sup>c</sup>Insomnia Impact Scale (Hoelscher, Ware, & Bond, 1993). <sup>d</sup>Beliefs and Attitudes about Sleep Scale (Morin, 1993). <sup>e</sup>Fatigue Severity Scale (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989). <sup>f</sup>Epworth Sleepiness Scale (Johns, 1991).



### *Sleep quality*

Sleep quality was used as an outcome measure in three of the four included studies (Riedel 1995; Lichstein 2001; and Fernando 2013). All of these studies used different measures and none used validated scales (Table 2-11). Riedel et al. (1995) used a scale rating the degree of sleep satisfaction for the preceding week from 1 (“not at all satisfied”) to 10 (“completely satisfied”). Lichstein et al. (2001) used a scale assessing perceived sleep quality from 1 (“very poor”) to 5 (“excellent”). Fernando et al. (2013) asked participants to compare their sleep to pre-treatment. All studies measured sleep quality at post treatment (four to six weeks). Both the Riedel et al. (1995) and Lichstein et al. (2001) studies also measured sleep quality at follow up (two months and one year, respectively). Although no identical scales were used, the Riedel et al. (1995) and Lichstein et al. (2001) studies were able to be combined for the purpose of meta-analysis.

The results in Figure 2-7 show that immediately post-treatment, the standard mean difference in sleep quality was 0.33 (95% confidence interval, -0.07 to 0.74). This figure represents 0.33 of one standard deviation and does not represent a significant difference between groups. Even with transformation back to the original rating scales, it would be unlikely to represent a significant clinical change in sleep quality. With only two studies for comparison, the results at follow up were combined despite there being a difference in timing of follow up. The overall result remains similar at follow up to post-treatment (Figure 2-8).

Fernando et al. (2013) dichotomised their results in order to compare treatment response in participants. These results were not included in the meta-analysis described above. They showed that 73% (16/22) of those in the sleep restriction group had better or much better sleep compared to 35% (8/23) in the control group. They reported a number needed to treat of 3 (95% confidence interval, 2 to 11). This suggested that sleep restriction led to an improvement in sleep quality over control.

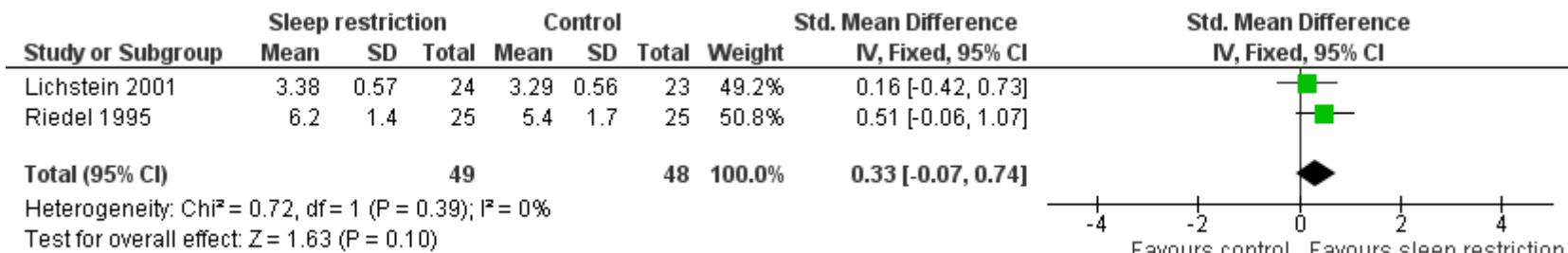


Figure 2-7: Meta-analysis comparing sleep quality at post-treatment for sleep restriction versus control groups

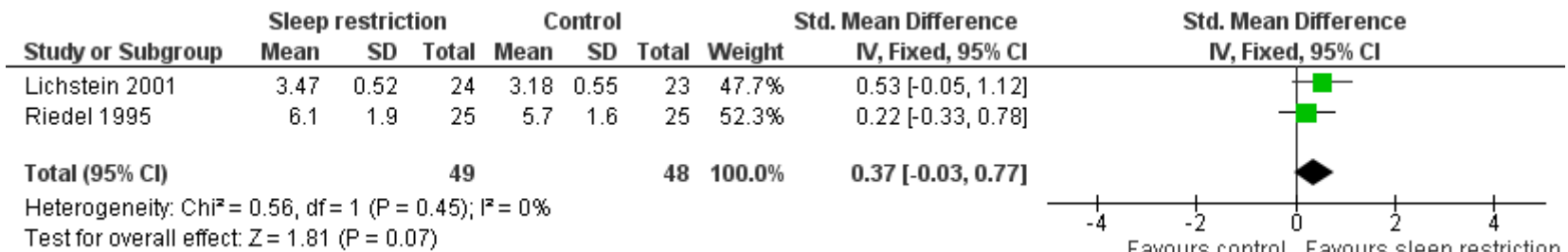


Figure 2-8: Meta-analysis comparing sleep quality at follow up for sleep restriction versus control groups

### *Sleep efficiency*

The results of the meta-analysis of the three studies that used sleep efficiency using sleep diaries are shown in Figure 2-9 and Figure 2-10 below. There was no significant difference between sleep restriction and control groups at any time point in the meta-analysis.

In addition to sleep diaries, Friedman et al. (2000) also measured sleep efficiency in all participants using actigraphy at post-treatment and follow up, and used polysomnography in a subgroup of participants ( $n = 12$  at post-treatment and  $n = 11$  at follow up). Lichstein et al. (2001) measured sleep efficiency using polysomnography at follow up all participants in addition to sleep diaries. Friedman et al. (2000) used the mean of two to four days of actigraphy recordings at each of the time points and found no significant difference between groups when measuring sleep efficiency at either of the time points. The meta-analysis of sleep efficiency measured by polysomnography at follow up is shown in Figure 2-11. There was no significant difference detected between the groups. However, when examined on its own, the Lichstein et al. (2001) study did detect a significant difference favouring sleep restriction at one year follow up. The combination of only two studies, with different follow up time points is a limitation of this meta-analysis.

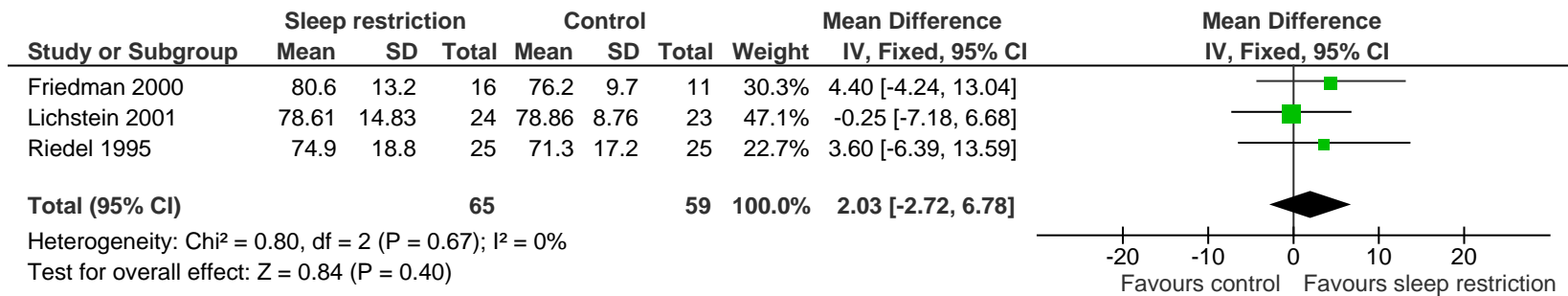


Figure 2-9: Meta-analysis comparing sleep diary sleep efficiency (ratio of time asleep/time in bed) at post-treatment for sleep restriction versus control groups

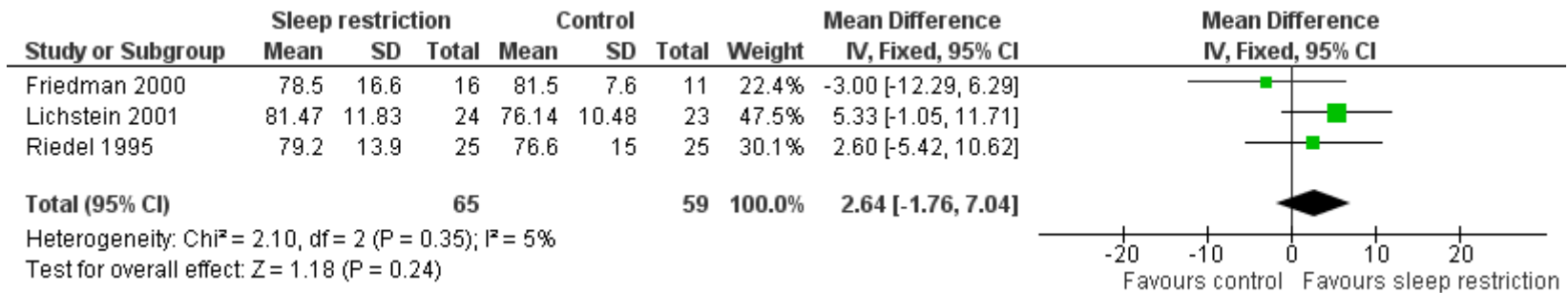
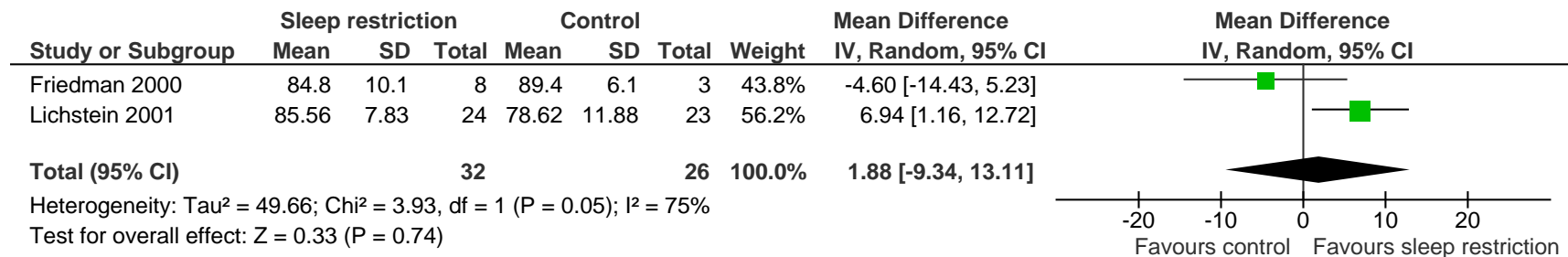


Figure 2-10: Meta-analysis comparing sleep diary sleep efficiency (ratio of time asleep/time in bed) at follow up for sleep restriction versus control groups



*Figure 2-11: Meta-analysis comparing sleep efficiency (ratio of time asleep/time in bed) at follow up as measured by polysomnography for sleep restriction versus control groups*

### *Sleep-onset latency*

Sleep-onset latency estimated using sleep diaries was similarly used as an outcome measure in three studies for both post-treatment and follow up (Riedel 1995; Friedman 2000; and Lichstein 2001). The overall estimate of effect at post-treatment was very mild and did not represent a statistically significant treatment effect between groups (reduction of time to sleep onset = -4.10 minutes, 95% confidence interval, -11.22 to 3.01; Appendix E). However, in the Riedel et al. (1995) study the baseline sleep-onset latencies between the two groups were not balanced (sleep restriction group = 60 minutes versus control group = 40 minutes). The meta-analysis assumes that due to adequate randomisation, the groups are balanced at baseline and that any change observed is due to a difference in treatment effect. A second analysis, excluding the Riedel et al. (1995) study remained non-significant. This showed a reduction of time to sleep onset of only -2.63 minutes (95% confidence interval, -10.53 to 5.27). At follow up, there was no significant difference in sleep-onset latency between groups measured by sleep diary, actigraphy, or polysomnography (Appendix E).

### *Wake after sleep onset*

Wake after sleep onset as measured by sleep diary was also used as an outcome measure in three studies for both post-treatment and follow up (Riedel 1995; Friedman 2000; and Lichstein 2001). As shown in Figure 2-12, the overall estimate of effect at post-treatment was modest, with participants in the sleep restriction group decreasing their time awake in bed after sleep onset by 13.22 minutes (95% confidence interval, -26.42 to -0.03). At follow up, a similar modest reduction in wake after sleep onset was shown (-14.62 minutes, 95% confidence interval -27.03 to -2.22; Appendix E). However, the modest improvement in wake after sleep onset was not supported by actigraphy which showed a slight increase in wake after sleep onset at post-treatment and follow up (Figure 2-13, Appendix E). Friedman et al. (2000) measured polysomnography at post-treatment in a subgroup ( $n = 8$ ). This showed a modest increase in wake after sleep onset. However, when both the Friedman et al. (2000) and Lichstein et al. (2001) studies were combined, no significant difference was seen using polysomnography at follow up (decrease in wake after sleep onset of 14.23 minutes, 95% confidence interval, -36 to 7.54; Appendix E).

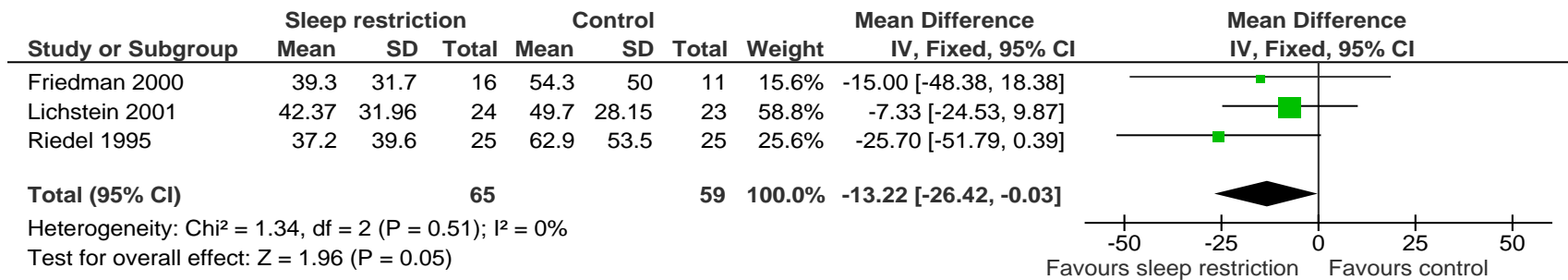


Figure 2-12: Meta-analysis comparing sleep diary wake after sleep onset at post-treatment for sleep restriction versus control groups

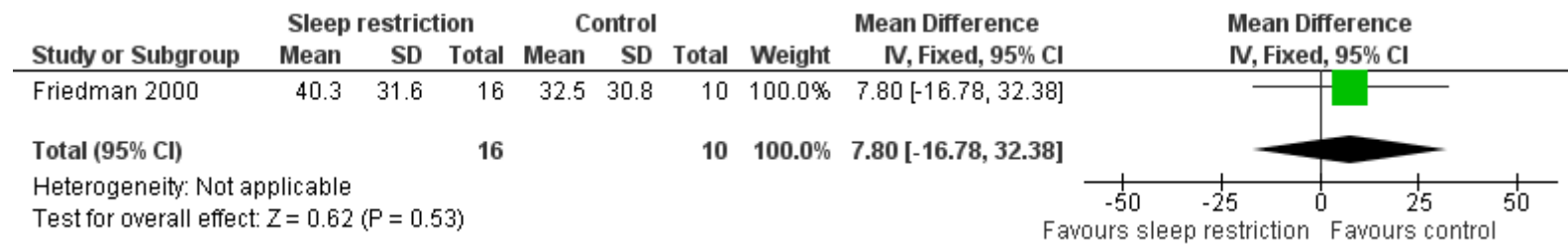


Figure 2-13: Meta-analysis comparing wake after sleep onset at follow up as measured by actigraphy for sleep restriction versus control groups

### *Total sleep time*

Total sleep time (sleep duration) was again used as an outcome measure in three studies for post-treatment and follow up analysis (Riedel 1995; Friedman 2000; and Lichstein 2001). The overall effect post-treatment was moderate, with the control group sleeping 44.91 minutes more per night than the sleep restriction groups (95% confidence interval, -69.00 to -20.81; Appendix E). This effect was supported by actigraphy in the Friedman (2000) study which showed the control group sleeping a similar amount of time more per night than the sleep restriction group (-43.60, 95% confidence interval, -79.11 to -8.09; Appendix E). A non-significant effect was seen in the small sample of the Friedman (2000) study who underwent polysomnography post-treatment (-48.30, 95% confidence interval, -101.55 to 4.95; Appendix E).

At follow up the difference between groups was no longer significant, with the control group sleeping 15.44 minutes more per night than the sleep restriction group (95% confidence interval, -38.68 to 7.80; Appendix E). When the long term follow up was analysed separately, the difference did not reach statistical significance, with the control group only sleeping 8.48 minutes more per night than the sleep restriction group (95% confidence interval, -43.70 to 26.74; Appendix E). When measured by actigraphy and polysomnography, the difference between groups was not significant either (Appendix E).



### *Daytime functioning*

Two studies used sleepiness as an outcome measure (Riedel 1995, Lichstein 2001). Riedel et al. (1995) used the Stanford Sleepiness Scale (Hoddes et al., 1973) which rates sleepiness during the afternoon on a scale from 1 (“feeling active and vital, alert, awake”) to 7 (“sleep onset soon, lost struggle to stay awake”). Lichstein et al. (2001) used the Epworth Sleepiness Scale (Johns, 1991) which rates likelihood of dozing during eight daytime situations on a scale ranging from 0 (“would never doze”) to 3 (“high chance of dozing”). The standardised mean difference was used to transform data for the purpose of standardised comparison. This analysis showed no significant difference between the groups at either post-treatment (0.15, 95% confidence interval, -0.25 to 0.55; Appendix E) or follow up (-0.05, 95% confidence interval, -0.45 to 0.35; Appendix E).

Fatigue was measured in only one of the included studies (Lichstein 2001). In this study the Fatigue Severity Scale (Krupp et al., 1989) was used both immediately post-treatment and at one year follow up. The Fatigue Severity Scale measures nine items which assess the level of intrusion of fatigue in daily life on a scale from 1 (“strongly disagree”) to 7 (“strongly agree”). There was no significant difference between groups regarding levels of fatigue at either of the time points (Appendix.E).

Lichstein et al. (2001) was also the only one of the included studies to use an outcome measuring other aspects of daytime functioning. The study used the Insomnia Impact Scale (Hoelscher et al., 1993) to assess the daytime impact of sleep. There was no significant difference between groups at either post-treatment or follow up (Appendix E).

### *Adverse effects*

None of the included studies reported on the adverse effects of treatment.

### **Risk of bias across studies**

Publication bias is a potential additional source of bias. This was unable to be formally assessed due to the small number of studies. Small sample size may have been another source of bias. A small sample size may lead to obscured differences between treatment groups and the unequal distribution of confounders.

### **Additional analyses**

No additional analyses were performed.

## **2.3.4 Discussion**

### **Summary of evidence**

There was evidence to suggest that sleep restriction reduces wake time after sleep onset at post-treatment and up to 1 year of follow up. However, there was insufficient evidence to show that sleep restriction significantly improves sleep quality and efficiency. There was also insufficient evidence of improvements in other sleep parameters, or sleepiness, fatigue, or insomnia impact.

### **Limitations**

This systematic review and meta-analysis was limited by the small number of trials conducted to date, and the small sample sizes. All of the three studies able to be combined in meta-analysis involved older adults recruited in the community. This also limits the ability to generalise the findings to other populations, such as adults of all age-groups in primary care. Only two of the four studies screened participants for obstructive sleep apnoea or periodic limb movements of sleep. If these conditions were present in the study participants, the population would be one with comorbid insomnia rather than primary insomnia. No studies investigated the potential adverse effects of sleep restriction therapy. The multiple comparisons used in the meta-analyses risk a type 1 error (Feise, 2002). It is possible that the significance of the reduction in wake after sleep onset in the sleep restriction compared to the control group was affected by a type 1 error (finding a significant difference when there is none).

### **Conclusions**

The results of this systematic review suggest that older adults may gain moderate benefit from sleep restriction therapy in reducing time awake overnight. However, the clinical meaningfulness of this finding is not clear. A lack of evidence about the potential harms of sleep restriction therapy also limits the wide spread recommendation of this treatment. However, it would be worthwhile to investigate sleep restriction therapy in adults, using a larger sample size. It would be important to correlate changes in sleep parameters with clinically meaningful outcomes and to ensure there are no significant harms

associated with the treatment. It would also be important to be mindful of the number of outcomes assessed, or the methods of minimising type 1 errors in planning statistical analyses.

## **2.4 Simplified Sleep Restriction**

Simplified sleep restriction is the modification of traditional sleep restriction that was used in the ReFRReSH trial described in the following chapter. The simplified sleep restriction protocol was developed specifically for the trial by the author. The theoretical basis for the development of the intervention is discussed below followed by a detailed explanation of the integrated theoretical model of simplified sleep restriction. Figure 2-14 shows the overall integrated model.

### **2.4.1 Theoretical basis for development of the intervention**

There are many predisposing and precipitating causes for insomnia (Section 2.1.3). The simplified sleep restriction model takes the theoretical stand that the behavioural processes are central to the maintenance of insomnia. The underlying logic for this assumption is discussed below. Elements of several theories were used to inform the development of the simplified sleep restriction model of behavioural change. These elements were: the concept of perceived behavioural control, the theory of self-efficacy, and the stimulus control theory. In the section below, these theoretical elements are discussed in turn and applied to the context of insomnia. This is followed by an explanation of their integration into the simplified sleep restriction model to promote change in sleep behaviours.

The most basic concept of sleep restriction is imposing a set of “normal” sleep conditions on those who no longer sleep normally. Normal sleep could be regarded as falling asleep relatively quickly after getting into bed in order to sleep, sleeping fairly solidly through the night, arising upon awakening in the morning, and feeling satisfactorily restored from the sleep with no significant negative daytime consequences attributed to the night’s sleep. These elements are the opposite of the conditions set for the general criteria for insomnia (American Sleep Disorders Association, 2005). The underlying core assumption is that those with insomnia no longer sleep well (“normally”) as their maladaptive behaviours prevent normal sleep. The maladaptive behaviours seen in those with insomnia include:

- going to bed when not sleepy
- spending excess time in bed awake (hoping to gain additional opportunity for sleep), and
- having erratic sleep schedules (for example, sleeping in after a poor night’s sleep).

## **Perceived behavioural control**

The concept of perceived control over performance of a behaviour (perceived behavioural control) is derived from the theory of planned behaviour described by Ajzen (Ajzen, 1991). This theory proposes that the intention to perform a particular behaviour is guided by three determinants: attitudes towards the behaviour, subjective norms, and perceived behavioural control (Ajzen, 1991). The determinant of perceived behavioural control was used when conceptualising the simplified sleep restriction model and therefore the discussion will focus on this aspect of the theory of planned behaviour. According to Ajzen (1991) “perceived behavioural control refers to people’s perception of the ease or difficulty of performing the behaviour of interest” (p. 183). He proposed that in general, a high level of perceived control should lead to a greater likelihood that a person will perform a behaviour. In a study looking at weight loss among college women Schifter and Ajzen (1985) hypothesised that successful weight loss could be predicted using the theory of planned behaviour. At the beginning of the study participants expressed their attitudes, subjective norms, perceived control, and intention regarding weight loss. Analysis of the results showed that perceived control over body weight alone was the best predictor of weight loss.

As applied to the development of the simplified sleep restriction intervention, the concept of behavioural control holds that it would be expected that simplified sleep restriction would improve sleep through enhancement of the perceived control the participant would have over the ability to change sleep patterns (improve sleep). The script used by the researcher to explain the intervention introduced the knowledge that it was possible to sleep better by changing sleep schedules and behaviours. Therefore, by increasing the perceived behavioural control of participants, it was expected they would be more likely to exert that control by following their sleep “prescription”. Perceived behavioural control is a slightly different concept to that of self-efficacy discussed below. Perceived behavioural control concerns the notion that people can change their sleep patterns through behavioural change. Self-efficacy concerns one’s own ability to make those changes.

## **The theory of self-efficacy**

The theory of self-efficacy was developed by Albert Bandura. He proposed that “self-efficacy beliefs are cognitions that determine whether health behaviour change will be initiated, how much effort will be expended, and how long it will be sustained in the face of obstacles and failures” (Bandura, 1977). More specifically, self-efficacy refers to the belief in one’s ability to exercise control over specific situations and events that affect one’s life (Bandura, 1977). Perceived self-efficacy in health behaviour (for example, smoking cessation, exercise) has been shown to predict attainment of health goals whereby those with higher levels of self-efficacy are more likely to achieve the desired goal (Strecher, DeVellis, Becker, & Rosenstock, 1986). The theory also proposes that a stressful situation (for

example, inability to sleep) leads to emotional arousal (for example, sleep anxiety) which becomes a source of information that can affect perceived self-efficacy (“I am so awake I will never be able to fall asleep”). Further, the theory proposes that high levels of arousal usually undermine performance (Bandura, 1977). A reduction in arousal therefore reduces the influence of the experience of arousal on perceived self-efficacy.

The theory of self-efficacy holds that simplified sleep restriction influences sleep quality by increasing self-efficacy leading to the behavior change (following a sleep schedule) that results in improved sleep (positive outcome). A positive feedback loop is created whereby following a sleep schedule (adhering to the sleep prescription) reinforces the participant’s confidence in the ability to make changes to achieve better sleep, thus further enhancing self-efficacy. The resulting improved sleep reduces emotional arousal (sleep anxiety). According to Bandura’s theory, reduced arousal leads to improved performance and the resulting increased self-efficacy (Bandura, 1977). Therefore, simplified sleep restriction therapy leads to increased self- efficacy both directly (adhering to the behavior change that improves sleep), and indirectly (less sleep anxiety).

Based on the theory of self-efficacy, specific elements were incorporated into the design of the simplified sleep restriction protocol to increase self-efficacy. Self-efficacy is initially enhanced by increasing knowledge using the simplified sleep restriction script (Appendix F). Specifically, the script provides information to support the notion that the participant has the ability to make behavioural changes that can improve sleep. Table 2-12 shows the elements of the script and the knowledge provided in order to enhance self-efficacy.

Table 2-12: Enhancing Self-Efficacy in “Simplified Sleep Restriction” Using a Standard Script

| Investigator’s script   | Knowledge provided to participant   |
|---|---|
| <p><i>“What happens when you have much more time in bed than actually asleep is that sleep can be shallower/poorer quality and more fragmented”</i></p>   | <p>That the effect of a volitional behaviour (spending long periods of time in bed) impacts upon sleep. Sleep has an internal locus of control.</p> |
| <p><i>“What we propose to do with this treatment is to set bedtimes and wake up times to corral sleep: to ‘scoop’ it all together so it is more condensed and occurs in a more solid chunk”</i></p>   | <p>If you follow specific behavioural instructions, sleep can be improved.</p>  |
| <p><i>“Gaining a regular bedtime schedule is important for helping to form a habit of good sleep...Having a schedule and a regular wake up time regardless of the previous night’s sleep means that if you have a poor night’s sleep but still get up at the same time regardless, you are likely to be a bit more tired or sleepy during the day – when bedtime comes, you will feel sleepier waiting until your prescribed bedtime and this additional ‘sleep pressure’ means you fall asleep faster and generally have a deeper sleep...So you can see that a poor night’s sleep actually feeds into the success of the programme”</i></p> | <p>Preventing negative interpretations of a poor night’s sleep or a feeling of daytime sleepiness which could erode sense of self-efficacy.</p>     |
| <p><i>“In order to make your sleep more efficient and hopefully more refreshing, we propose that for the next two weeks, we attempt to retrain your brain to sleep better”</i></p>  | <p>It is possible to train the brain to sleep better.</p>   |
| <p><i>“Limiting the time you are allowed in bed to correlate closely with the actual time you are spending sleeping is simple in theory but can be challenging in practice. Some people have a hard time forcing themselves to stay awake in the first phase of treatment. However, those who can stick with it often find it remarkably effective”</i></p>   | <p>Preventing negative interpretations of no immediate change in sleep.</p>   |

Table 2-13 shows three key strategies for increasing self-efficacy incorporated into the design of the simplified sleep restriction intervention (Rimer & Glanz, 2005).

*Table 2-13: Strategies for Enhancing Self-Efficacy in the Design of the “Simplified Sleep Restriction” Intervention*

| <b>Strategy</b>                         | <b>Example</b>  |
|---|---|
| ▪ Setting incremental goals             | The “sleep prescription” uses a modification of the traditional sleep restriction procedure. Excess time in bed is reduced by 50% (rather than 100%) at the initial visit and then further reduced if sleep is not sufficiently improved at the second visit. |
| ▪ Behavioural contracting               | Written instructions regarding sleep prescription.  |
| ▪ Monitoring and internal reinforcement | Sleep self-adjustment algorithm.  |

### **The theory of stimulus control**

Bootzin’s theory of stimulus control has been described previously (in section 2.1.3) (Bootzin et al., 1991). Briefly, by limiting the time allowed in bed, sleep restriction (and the simplified sleep restriction model) aimed to re-establish the bed time, bedroom, and bed as strong conditioned cues for sleep rather than arousal.

### **2.4.2 The integrated theoretical model of simplified sleep restriction**

Figure 2-14 shows how the elements of theory were incorporated into the design of the simplified sleep restriction intervention. The construct is broadly arranged using chronological continuum of: the introduction of knowledge (the script), the proscribed behaviour change (the sleep prescription) and the learned skill of self-management (sleep self-adjustment algorithm). The script uses the theoretical constructs of perceived behavioural control and self-efficacy to motivate behaviour change (following the sleep prescription). Providing the personalised prescription itself is proposed to increase motivation to make the behaviour changes by creating the expectation that sleep can improve if the instructions are

followed. Making the behavioural changes defined in the sleep prescription leads both directly and indirectly to improved sleep.

The indirect routes are via a reduction in effort directed at lying in bed and trying to fall asleep and via a reduction in arousal. Reduction in arousal occurs as a result of the sleep prescription (leaving less time to lie in bed awake with busy thoughts and sleep anxiety), and due to the reduction in effort directed at trying to sleep (which in itself is arousing and anxiety-provoking). The resulting improved sleep leads to a change in beliefs about sleep (the ability to sleep, that quality is better than quantity, that going to bed late is ok) that further reinforces the behaviour change. Improved sleep also leads to a reduction in arousal and an increase in self-efficacy beliefs. The sleep self-adjustment algorithm provides a tool for self-management of sleep according to the basic principles of sleep restriction when the contact with the general practitioner is finished. It also provides a means of self-evaluation of the outcomes of the behavioural changes. Either a positive or negative assessment of outcomes would lead to an increase in perceived behavioural control because the tool provides a mechanism to adjust the sleep schedule for any outcome scenario. This sense of control then leads to increased self-efficacy which in turn feeds back to positively influence behaviour change.

In summary, the intervention of simplified sleep restriction is a modification of the traditional principle of sleep restriction. The modifications involve referencing theoretical concepts about human behaviour and behavioural change. The specific concepts utilised in the model were: the theory of perceived behavioural control, the theory of self-efficacy, and the theory of stimulus control. Three unique tools were developed to deliver the intervention: the script, the sleep prescription, and the sleep self-adjustment algorithm.



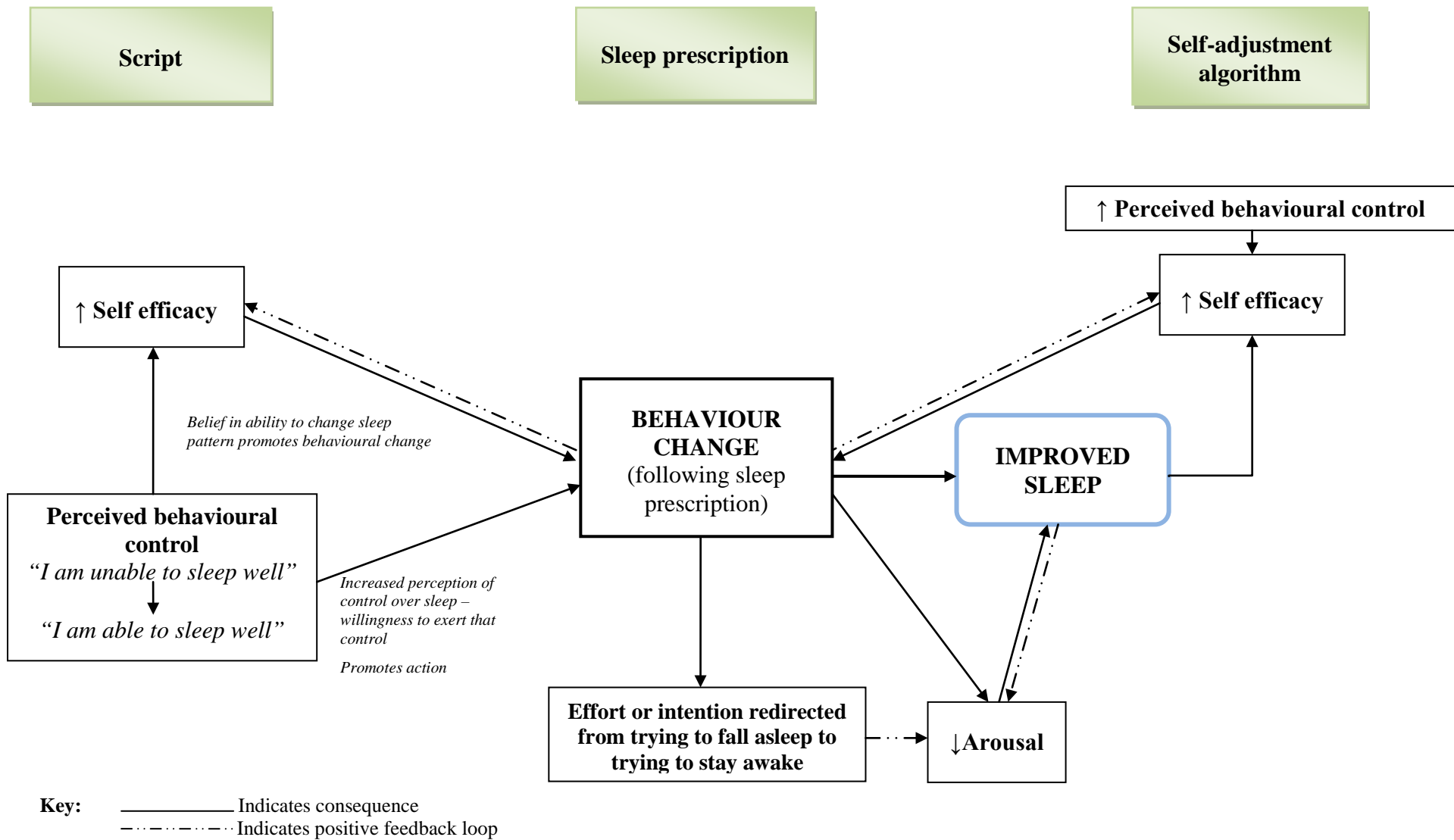


Figure 2-14: Integrated theoretical model of simplified sleep restriction

## Chapter 3 Methods

### 3.1 Introduction

Primary insomnia refers to insomnia that is not better explained by, or does not occur exclusively during the course of another condition such as a diagnosable sleep disorder or medical condition (American Psychiatric Association, 2000). To date there are no randomised controlled trials of sleep restriction for the treatment of primary insomnia where treatment is delivered during the primary care consultation. Yet a simply delivered sleep restriction intervention would be ideal for the primary care setting as it can be delivered in a relatively short space of time. The effectiveness of simplified sleep restriction as a treatment for primary insomnia in the primary care setting was assessed by the author in the ReFReSH trial (Restriction For Reorganisation of Sleep Habit). This was a randomised controlled trial of sleep restriction in those with primary insomnia recruited from the primary care setting. It was designed to represent an intervention that can be delivered by the general practitioner during a consultation. This chapter describes the methods of the ReFReSH trial.

The primary hypothesis underlying the trial was that poor sleep habits in those with primary insomnia could be managed using the behavioural technique of sleep restriction (also known as bed time restriction) without the other components of a cognitive behavioural therapy (CBT-I) package. The poor sleep habits of primary insomnia were theorised to be a combination of circadian disruption via improper sleep scheduling and homeostatic disruption via reduced sleep drive (Spielman, Caruso, et al., 1987; C. M. Yang et al., 2006) (Section 2.2.3). That is, the poor sleep habits were primarily considered to be behavioural. The secondary hypothesis was that cognitive components of insomnia exert less inhibitory effect on sleep if a measure of success is first obtained through using a sleep restriction protocol. That is, if one is sleeping better, confidence is gained in the intrinsic ability to sleep and there are less negative cognitions about sleep. Thus, it is hypothesized that the cognitive components may not need to be formally addressed as a separate component of treatment (as they are in cognitive behavioural therapy for insomnia). The behavioural treatment of sleep restriction would thus fall within the existing skill set of the general practitioner with minimal additional training, as opposed to CBT-I which requires additional training and consultation time. The general practitioner would then be able to manage the large proportion of those with primary insomnia, referring only difficult or refractory cases to specialists. If general practitioners were confident in their ability to manage insomnia, it may also prompt more enquiry or “case finding” of insomnia in the routine consultation.

The randomised controlled trial was designed to answer the research question: “Is sleep restriction an effective and safe treatment for primary insomnia in the primary care setting?” The clinical significance of the outcomes in this context was considered to be reflected in improved subjective perception of sleep quality (as insomnia is essentially subjectively defined) and/or in improvements in the patient’s global “wellbeing” as assessed by sleepiness, fatigue and mood outcomes. Therefore, the primary outcome of the ReFReSH trial was sleep quality where change in sleep quality was subjectively and objectively assessed over a six month period. Secondary measures included change in sleepiness, fatigue, sleep parameters, depression, and anxiety assessed using validated scales. The measures used were chosen with reference to standard insomnia research recommendations adapted to be relevant and appropriate for the primary care setting (Buysse et al., 2006).

Monitoring of the potential harms of the intervention was also undertaken. The potential harms associated with sleep restriction were hypothesized to relate to the initial period of mild partial sleep deprivation incurred as a consequence of the initial restriction in bed time allowance at the beginning of the treatment protocol. This mild sleep deprivation could potentially cause increased sleepiness leading to accident or injury, or to physiological stress potentially manifesting as dizziness, shortness of breath or angina (Kyle et al., 2013). Any clinically significant increase in sleepiness, fatigue, depression or anxiety would also be considered a possible harm of the treatment.

The methods and reporting of the results adheres to the requirements of the Consolidated Standards of Reporting Trials (CONSORT) (Boutron et al., 2008). The CONSORT statement is an evidence-based, minimum set of recommendations for reporting randomised controlled trials.

The adaptation of the intervention and the design and conduct of the ReFReSH trial was undertaken by the author, who is also a part-time general practitioner in Auckland, New Zealand.

### **3.2 Aims**

The aims of this trial were:

- To evaluate the effectiveness of sleep restriction in the treatment of primary insomnia in the primary care setting;
- To identify any harms or safety concerns that may be attributed to the sleep restriction intervention.

### **3.3 Design**

The individual parallel design randomised controlled trial of simplified sleep restriction as a treatment for primary insomnia was designed and refined by the author prior to the trial commencing in March 2009. Simplified sleep restriction plus modified sleep hygiene was compared with a control consisting of modified sleep hygiene instructions alone. Major assessments were conducted at baseline and at a six month follow-up. A brief postal survey assessed subjective sleep quality at three months. All participants were instructed to follow their treatment advice for the entire six month study period. Assessment of potential harms occurred at baseline, at three weeks and at six months. The study setting and population, protocol, outcome measures, interventions, randomisation procedures, sample size calculations, data analysis and safety/harms monitoring are outlined below.

### **3.4 Participants**

The participants were adults aged 16 to 75 years old with primary insomnia recruited from multiple general practices between March 2009 and May 2012.

#### **3.4.1 Study population**

The study catchment area was located in the Auckland region of New Zealand. Approximately one third of New Zealand's population lives in the Auckland region (<http://communities.co.nz/AucklandRegion/AucklandRegion.cfm>). General practice clinics within the Auckland District Health Board (ADHB) catchment area were approached to participate as "recruitment practices" (Appendix F). All the practices in this area were urban practices except for those on Waiheke Island. The ADHB catchment area serves a population of approximately 458,000. ([http://www.adhb.govt.nz/about/population\\_stats.htm](http://www.adhb.govt.nz/about/population_stats.htm) accessed 4/12/11).

#### **3.4.2 General practice inclusion and exclusion criteria**

An established database of general practices in the greater Auckland region was used to generate the list of practices located in the ADHB catchment area. This list was compiled and held by the Department of General Practice and Primary Health Care at the University of Auckland. The version used for this trial had been updated in 2007. Therefore, practices must have appeared on this list to have been eligible for inclusion into the study. Practices were included in the trial recruitment if the practice manager and doctors agreed to participate. Practices were excluded if they did not have the MedTech32 practice management system (<http://www.medtechglobal.com/global/products-2/medtech32-global.html>), were solely servicing a retirement village, or were an accident and medical (A & M) clinic. Fourteen random practices were enlisted as "recruitment practices". In addition to

recruiting through these recruitment practices, faxes were sent to all practices in the Auckland and Waitemata District Health Board catchment areas (Appendix F) appearing on the general practice database introducing the study to general practitioners and providing investigator contact details for interested patients.

### **3.4.3 General practitioner and practice recruitment**

General practice clinics from the ADHB catchment area were listed in alphabetical order within geographic quadrants and sequentially numbered. A random number sequence was used to determine the order of recruitment. Practice managers were sequentially contacted by telephone or email. If contact was not obtained by two telephone attempts, an information pack was delivered to the practice. If email contact was made, the information pack was included as an attachment. Practices were contacted and recruited according to resource availability. Generally, recruitment of each practice would begin before the next practice was contacted and recruitment commenced. This rolling recruitment of practices continued until adequate participants were recruited for the trial.

Once the general practitioners (GPs) in a practice consented to participation, an electronic query was run on the MedTech practice management system to list patients aged between 16 and 75 years for each provider (general practitioner). Using a computerised randomly generated sequence, this list was initially reduced to 30% for each provider. After recruitment from the first three practices, this procedure was amended to include generating a list of all patients aged between 16 and 75 years to boost numbers of potential participants from each practice. This was because the response rate was not as high as originally anticipated, and the proportion excluded was higher than initially estimated.

### **3.4.4 Patient recruitment**

The GPs were asked to review their patient list to exclude those they considered unsuitable for participation according to the listed exclusion criteria. As a guide to general practitioners it was suggested that those with unstable physical or mental health, unable to speak English, living outside of Auckland, dementia or intellectual incapacity, and any untreated known sleep problem other than primary insomnia would probably not be suitable for the study. The GPs signed a master copy of their letter, which introduced the study on behalf of the University of Auckland researchers and asked about insomnia symptoms (Appendix G). Table 3-1 lists the questions included in the letter.

The letter also asked patients to fill in their name and contact details if they had poor sleep and wished to participate further. This enabled the researchers to obtain the patient details with their explicit consent. The letter was photocopied and mailed out along with a freepost envelope for the replies to be sent to The University of Auckland Sleep Study (the author). The generation of the patient lists and the mail out procedure was performed by either a member of the practice who received reimbursement for

this task, or by the study researcher (the author or research assistant MD – also a general practitioner) as an honorary practice member after signing a confidentiality agreement.

*Table 3-1: Questions Asked in Initial Mail-Out Letter to Patients During the ReFRreSH Trial Recruitment*

| <b>Question</b>   | <b>Possible responses</b>  |
|---|--|
| 1) During the past month how would you rate your sleep quality overall? <sup>a</sup>  | Very good<br>Fairly good<br>Fairly bad<br>Very bad                                 |
| 2) Do you have trouble with your sleeping (i.e. difficulty initiating sleep, difficulty maintaining sleep, waking up too early, or sleep that is non-restorative or poor in quality) such that it interferes with your function the following day? <sup>b</sup> | Yes<br>No  |
| 3) Does this occur 3 or more times per week? <sup>b</sup>   | Yes<br>No<br>Not applicable  |
| 4) Does your difficulty sleeping occur even when you give yourself adequate opportunity to sleep? (that is, allowing yourself enough time to have a good sleep and not “burning the candle at both ends”) <sup>b</sup>  | Yes<br>No<br>Not applicable  |
| 5) How worried/distressed are you about your current sleep problem? <sup>c</sup>  | Not applicable or not worried<br>A little<br>Somewhat<br>Much<br>Very much worried |

*Note.* <sup>a</sup>Subjective sleep quality component of Pittsburgh Sleep Quality Index (Buysse et al., 1989)

<sup>b</sup>*International Classification of Sleep Disorders (Second Edition)* general diagnostic criteria for insomnia (American Sleep Disorders Association, 2005) <sup>c</sup>Item five of the Insomnia Severity Index (Bastien et al., 2001; Morin, 1993)

### 3.4.5 Patient inclusion and exclusion criteria

The inclusion and exclusion criteria described below were designed to meet the Research Diagnostic Criteria (RDC) for primary insomnia (Edinger et al., 2004).

#### **Inclusion criteria**

Table 3-2 lists the patient inclusion criteria. Participants were required to fulfill general criteria for insomnia as specified by the *International Classification of Sleep Disorders (Second Edition) (ICSD-2)* (American Sleep Disorders Association, 2005). These criteria define insomnia as a complaint of difficulty initiating sleep, difficulty maintaining sleep, waking up too early, or sleep that is chronically non-restorative or poor in quality, that occurs despite adequate circumstances and opportunity for sleep, and causes at least one form of daytime impairment (American Sleep Disorders Association, 2005). In addition, patients also had to fulfill insomnia minimum frequency and severity criteria. The insomnia also had to be of at least six months duration to be considered chronic insomnia as per research convention (Espie et al., 2007; Morin, Vallieres, et al., 2009). These frequency, severity, and duration criteria are in line with international recommendations for the assessment and study of insomnia (Buysse et al., 2006; Lichstein, Durrence, Taylor, Bush, & Riedel, 2003). In addition, participants were required to score greater than five on the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989). This cut-off on the PSQI has been shown to have nearly 90% diagnostic accuracy (89.6% diagnostic sensitivity and 86.5% specificity) in identifying significant sleep disturbance by distinguishing between “good” and “poor” sleepers (Buysse et al., 1989). Subjects were also required to have a level of worry or distress about their sleep problem rating at least two on item five of the Insomnia Severity Index (ISI) (i.e. being “somewhat” worried to “very much worried”) (Bastien et al., 2001; Morin, 1993). Similar inclusion criteria protocols have been used to identify the primary insomnia population in recent research (Espie et al., 2007; Morin, Vallieres, et al., 2009).

Once the researchers received a reply that fulfilled insomnia criteria (“yes” to the three core insomnia questions) and indicated significant worry or distress about the sleep problem a comprehensive questionnaire (Q2) and patient information sheet was sent out to the patient (Appendices H, I). The purpose of the Q2 was to diagnose the cause of the insomnia. The flowchart of participant recruitment is presented in Figure 3-1.

Table 3-2: Patient Inclusion Criteria for the ReFRoSH Randomised Controlled Trial

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**Inclusion criteria**

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- 1) Aged 16 to 75 years old
- 2) Living in Auckland region
- 3) Difficulty initiating and/or maintaining sleep, comprising sleep onset latency  $\geq 30$  minutes and/or wake after sleep onset  $\geq 30$  minutes, 3 or more nights per week despite adequate opportunity and circumstance for sleep<sup>ab</sup>
- 4) Worry or distress about the sleeping problem (rating  $\geq 2$  on item 5 of the Insomnia Severity Index<sup>c</sup>)
- 5) Insomnia duration longer than 6 months<sup>de</sup>
- 6) Score of  $>5$  on the Pittsburgh Sleep Quality Index<sup>f</sup>
- 7) Primary insomnia diagnosis

Note. <sup>a</sup>(American Sleep Disorders Association, 2005) <sup>b</sup>(Buysse et al., 2006) <sup>c</sup>(Bastien et al., 2001) <sup>d</sup>(Espie et al., 2007) <sup>e</sup>(Morin, Vallieres, et al., 2009) <sup>f</sup>(Buysse et al., 1989)

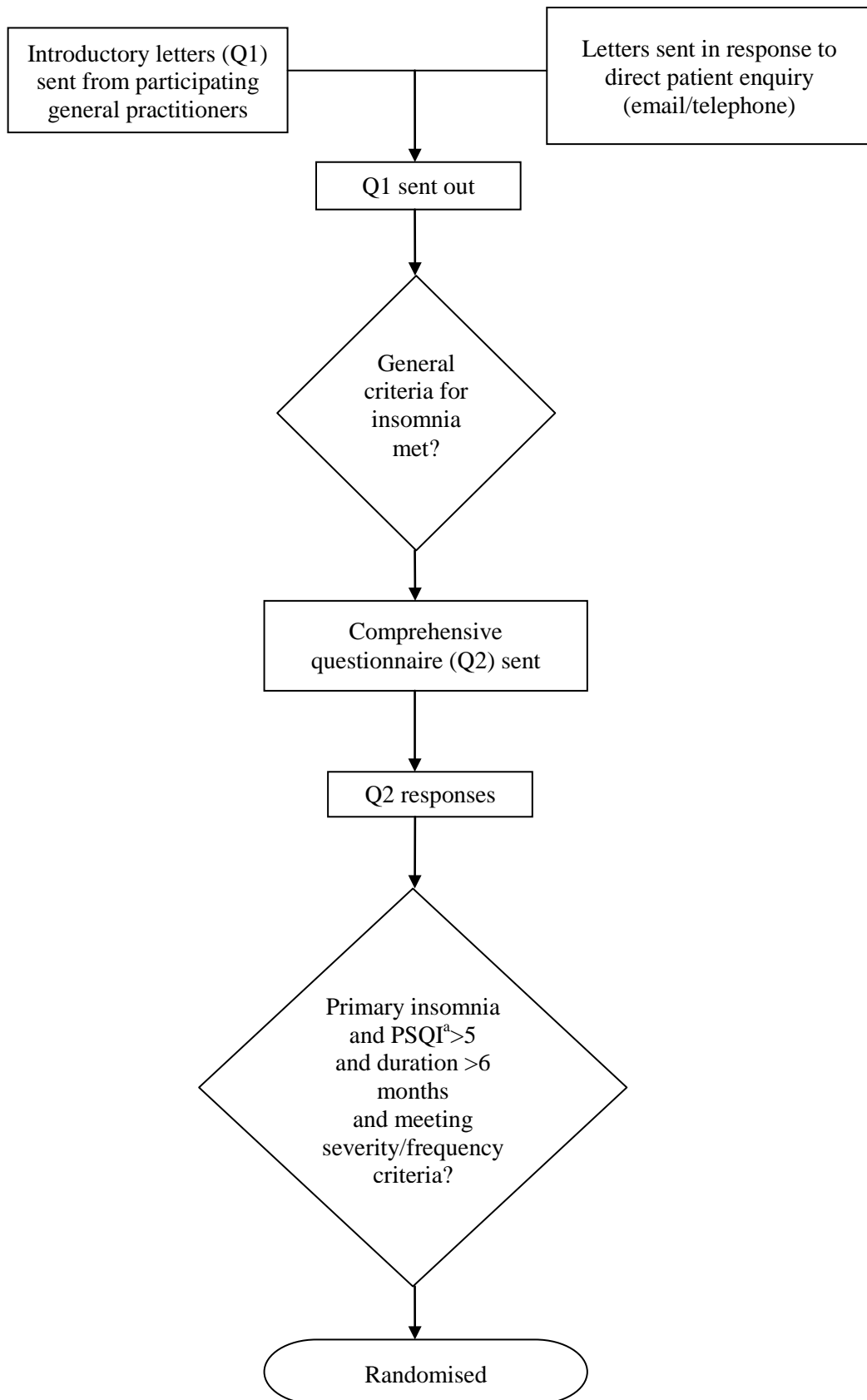
**Exclusion criteria**

The exclusion criteria were designed to ensure those participating in the trial suffered from primary insomnia according to research diagnostic criteria (Edinger et al., 2004) and were fit for participation in the trial. Patients were excluded if their Q2 questionnaire responses indicated: the likely presence of another sleep disorder (e.g. obstructive sleep apnoea or restless legs syndrome); a heart attack or stroke in the previous six months; ongoing chest pains, dizziness, fainting attacks or shortness of breath; an Epworth Sleepiness Score (ESS)  $>10$  (Johns, 1991); moderate to severe depression indicated by PHQ-9 score  $\geq 9$  (Kroenke, Spitzer, & Williams, 2001); suicidality (assessed by the PHQ-9 questionnaire); moderate to severe anxiety indicated by GAD-7 score  $\geq 8$  (Kroenke, Spitzer, Williams, Monahan, & Lowe, 2007; R.L. Spitzer, Kroenke, Williams, & Lowe, 2006); shift work; current pregnancy; or breast-feeding. Furthermore, a patient was excluded if the regular use of prescription sleep medications was indicated and the patient was unwilling or unable to discontinue regular use during the study. If the patient had an occupation where increased period of sleepiness or fatigue would be especially risky (such as driving a passenger or heavy vehicle; working with machinery; or a surgeon) the patient was excluded if it was not possible to start the trial during a period of leave. Patients were also excluded if



they had an abnormal physical examination increasing the possibility of a secondary cause for insomnia such as obstructive sleep apnoea or undiagnosed cardiorespiratory abnormality. Physical exclusions included the presence of two or more of the following: a body mass index (BMI) >35 (severe obesity), neck circumference >42 centimeters (Flemons, Whitelaw, Brant, & Remmers, 1994; Kryger, Roth, & Dement, 2011), reduced oropharyngeal size (Mallampati score of 3 or 4 (Mallampati et al., 1985)); abnormal facial morphology or abnormal cardiorespiratory exam. Finally, patients were excluded if they were unable to read or write English or were unwilling to complete the informed consent process.

Patients were not excluded if they were on medications known to affect sleep such as selective serotonin reuptake inhibitor antidepressants (for example, fluoxetine and paroxetine) as long as they were below the cut-off threshold for current depression and anxiety, were stable on these medications, and were not planning on discontinuing medication during the study period.



<sup>a</sup>Pittsburgh Sleep Quality Index (Buysse, Reynolds III, Monk, Berman, & Kupfer, 1989)

Figure 3-1: Flowchart showing outline of participant recruitment in the ReFRoSH trial

### **Method for assessing the presence of other sleep disorders**

Primary insomnia is a diagnosis of exclusion (American Sleep Disorders Association, 2005). Polysomnography (PSG)<sup>2</sup> is not required for the standard evaluation of insomnia as diagnosis of insomnia relies on a subjective complaint (Reite, Buysse, Reynolds, & Mendelson, 1995). Use of polysomnography for the purpose of confirming participants were suffering from primary insomnia rather than another sleep disorder (such as obstructive sleep apnoea or restless legs syndrome for which polysomnography is useful in diagnosis) was not used in this trial due to resource constraints and as the trial was designed to reflect the “real world” situation for GPs who would be basing the majority of their primary insomnia diagnoses on history and physical examination alone. There were no simple, validated, universally recognised questionnaires to evaluate the presence of the more prevalent sleep disorders such as obstructive sleep apnoea in general practice at the time of recruitment. For this reason, a pragmatic approach was taken to evaluating the presence or absence of sleep disorders for the purpose of finding participants with primary insomnia. The diagnosis of sleep disorders comprising exclusion criteria are detailed in Appendix J.

#### ***Obstructive sleep apnoea***

The prevalence of obstructive sleep apnoea in the New Zealand primary care population is estimated to be 9% (Bruce Arroll et al., 2012). A high body mass index (BMI), increasing age, male sex, excessive daytime sleepiness and loud snoring are all risk factors for obstructive sleep apnoea (Buysse et al., 2006). Therefore, patients were excluded if they had a BMI greater than 35 or their score on the Epworth Sleepiness Scale (ESS) was greater than 10 (Johns, 1992). Additional screening for sleep apnoea included the physical examination of tonsillar size and palate position using the Mallampati score and measurement of the neck circumference (Mallampati et al., 1985; Nuckton, Glidden, Browner, & Claman, 2006). Patients were excluded if their Mallampati score was greater than two or their neck circumference was greater than 42 centimeters.

There was a slight variation in procedure early in recruitment regarding exclusions based on the ESS score. Initially, participants were automatically excluded if their ESS score at the baseline appointment was >10 (regardless of the presence or absence of other risk factors for obstructive sleep apnoea). However, it was noticed that several potential participants who may well have had primary insomnia were excluded from participating in the trial solely on the basis of having an initial ESS score >10, and often despite having an ESS ≤10 on the second questionnaire (Q2). After discussion with the trial supervisor (RE), the decision was made to include those with ESS >10 at the baseline appointment as

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<sup>2</sup>Polysomnography the polygraphic recording during sleep of multiple physiologic variables, both directly and indirectly related to the state and stages of sleep, to assess possible biologic causes of sleep disorders. Mosby's Medical Dictionary, 8th edition. © 2009, Elsevier

long as the other risk factors were not present. The final criteria used for excluding patients on the basis of high risk of obstructive sleep apnoea are summarised in Table 3-3.

*Table 3-3: Exclusion Criteria for Probable Obstructive Sleep Apnoea in the ReFRaSH Trial*

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**Exclusion criteria**

---

- ESS >10<sup>a</sup>

*and*

- Presence of  $\geq 1$  of the below risk factors:
  - Mallampati score of 3 or 4<sup>bc</sup>
  - Neck circumference >42 cm<sup>d</sup>
  - BMI<sup>e</sup> >35

*Note.* <sup>a</sup>ESS: Epworth Sleepiness Scale (Johns, 1991) <sup>b</sup>(Mallampati, Gatt et al. 1985) <sup>c</sup>Nuckton, Glidden et al. 2006) <sup>d</sup>(Flemons et al., 1994)) <sup>e</sup>BMI: Body Mass Index kg/m<sup>2</sup>

### ***Restless legs syndrome and periodic limb movements of sleep***

The prevalence of restless legs syndrome (RLS) in the primary care population is estimated to be around 20% (Bruce Arroll et al., 2012). RLS refers to unpleasant sensations in the legs (or arms) that cause the patient to want to move and the sensations are relieved by movements. RLS often occurs when lying in bed and can interfere with falling asleep. RLS is considered to be reliably assessed by history and questionnaire (Buysse et al., 2006; Walters, 1995). The corresponding questions used in the second questionnaire (Q2) were derived from the *International Classification of Sleep Disorders (Second Edition) (ICSD-2)* diagnostic criteria for restless legs syndrome (American Sleep Disorders Association, 2005).

Periodic limb movements of sleep (PLMS) are repetitive stereotyped movements of the lower limbs that occur during sleep. PLMS are more difficult to assess on clinical history alone (Buysse et al., 2006). Classification according to *ICSD-2* requires polysomnography for diagnosis (American Sleep Disorders Association, 2005). However, PLMS are of uncertain clinical significance and although the majority of those with RLS will have PLMS, only a minority of those with PLMS alone will have insomnia (Vaughan & D'Cruz, 2011). Therefore, the questions used to screen for RLS were considered

a pragmatic way to exclude those with clinically meaningful PLMS in the absence of polysomnography.

### ***Circadian rhythm disorders***

The prevalence of circadian rhythm disorders (“advanced sleep phase” or “delayed sleep phase”) in the general population is estimated to be close to 1% (Ohayon & Smirne, 2002). The prevalence of delayed sleep phase disorder in the primary care setting is approximately 2% (Bruce Arroll et al., 2012). Circadian rhythm sleep disorders were assessed using symptom questionnaires based on *ICSD-2* diagnostic criteria (American Sleep Disorders Association, 2005) and sleep time information.

### ***Other exclusions***

Patients with other conditions or circumstances potentially explaining the occurrence of the insomnia complaint were excluded on the basis of questions designed to reflect the *ICSD-2* diagnostic criteria for insomnia (American Sleep Disorders Association, 2005). These conditions or circumstances included shift work, pregnancy, breastfeeding or within six months of giving birth, frequent menopausal hot flushes, medical health problems, sleep walking, bruxism (teeth grinding), nightmares, nocturnal panic and illicit substance use. Potential alcohol dependence was assessed using the CAGE brief screen for alcoholism (Ewing, 1984). Using this questionnaire a positive response to  $\geq 2$  out of 4 questions leads to a high index of suspicion for alcoholism and was therefore an exclusion criteria. Wording of the questions can be seen in the second questionnaire (Q2) in the Appendix H.

### **Baseline appointment**

Those fulfilling the criteria for primary insomnia were then invited by telephone call or email to a 20 minute meeting where the author met with the participant and the trial was discussed. This appointment was held at a mutually convenient location. Participants had an opportunity to ask any questions relating to the participant information sheet or the trial in general. Following this process, written informed consent was obtained (Appendix K). The participants were then issued with an Actiwatch<sup>3</sup> to wear continuously for two weeks and a sleep diary to complete daily over the same period. The participants were instructed on the use of the Actiwatch and a handout was given for reference (Appendix L). Accurate recording of the sleep diary was explained with written material according to instructions described by Morin (Morin, 1993) (Appendix M). The participants were instructed to carry on usual daily life and sleep habits during this data collection period. A meeting time was set for the baseline measures appointment after the two weeks of continuous data collection. In some circumstances appointments were held in the home of the participant.

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<sup>3</sup> Actiwatch – see description in the section on Materials and Measures p. 104

The Actiwatch and completed sleep diary were collected at the baseline measures appointment. This appointment (performed by the author) lasted approximately 70 minutes and consisted of analysis of sleep diary data, brief medical history, brief physical exam, and completion of baseline questionnaires prior to randomisation. The brief, clothed physical examination consisted of: resting blood pressure and pulse, height, weight, body mass index, neck circumference, facial inspection, tonsil/palate inspection and brief cardiorespiratory exam (Appendix N). The baseline questionnaire recorded sleep quality (PSQI (Buysse et al., 1989) and ISI (Morin & Espie, 2003)), sleepiness (ESS (Johns, 1991)), depression (PHQ-9 (Kroenke et al., 2001)), anxiety (GAD-7 (R.L. Spitzer et al., 2006)), and fatigue scores (Flinders Fatigue Scale (Grasidar et al., 2007)) (Appendix O). Where sleep diary inclusion criteria were met (at least 30 minutes sleep-onset latency and/or 30 minutes wake after sleep onset, occurring on at least 3 nights per week), and no further exclusion criteria were identified in regards to medical, mental or physical health, participants were enrolled in the trial and received a group allocation. Sections 3.7 and 3.8 provide a detailed description of randomisation and blinding procedures.

### **3.5 Intervention**

After randomisation, both the “simplified sleep restriction” group and the control group received verbal advice at a visit with the author. All participants also received a “good sleep guide” handout, with sleep hygiene information such as avoiding caffeine, relaxing before bedtime and creating a pre-bed routine (Hauri, 1991), a handout on “safety” and “drowsy driving”, and a blank two week sleep diary (Appendices M, P, Q, R). Both groups were asked to continue sleep diaries for a further two weeks after baseline, before meeting with the author to discuss progress at a second visit during the third week. The participant flow through the study is summarised in Figure 3-2.

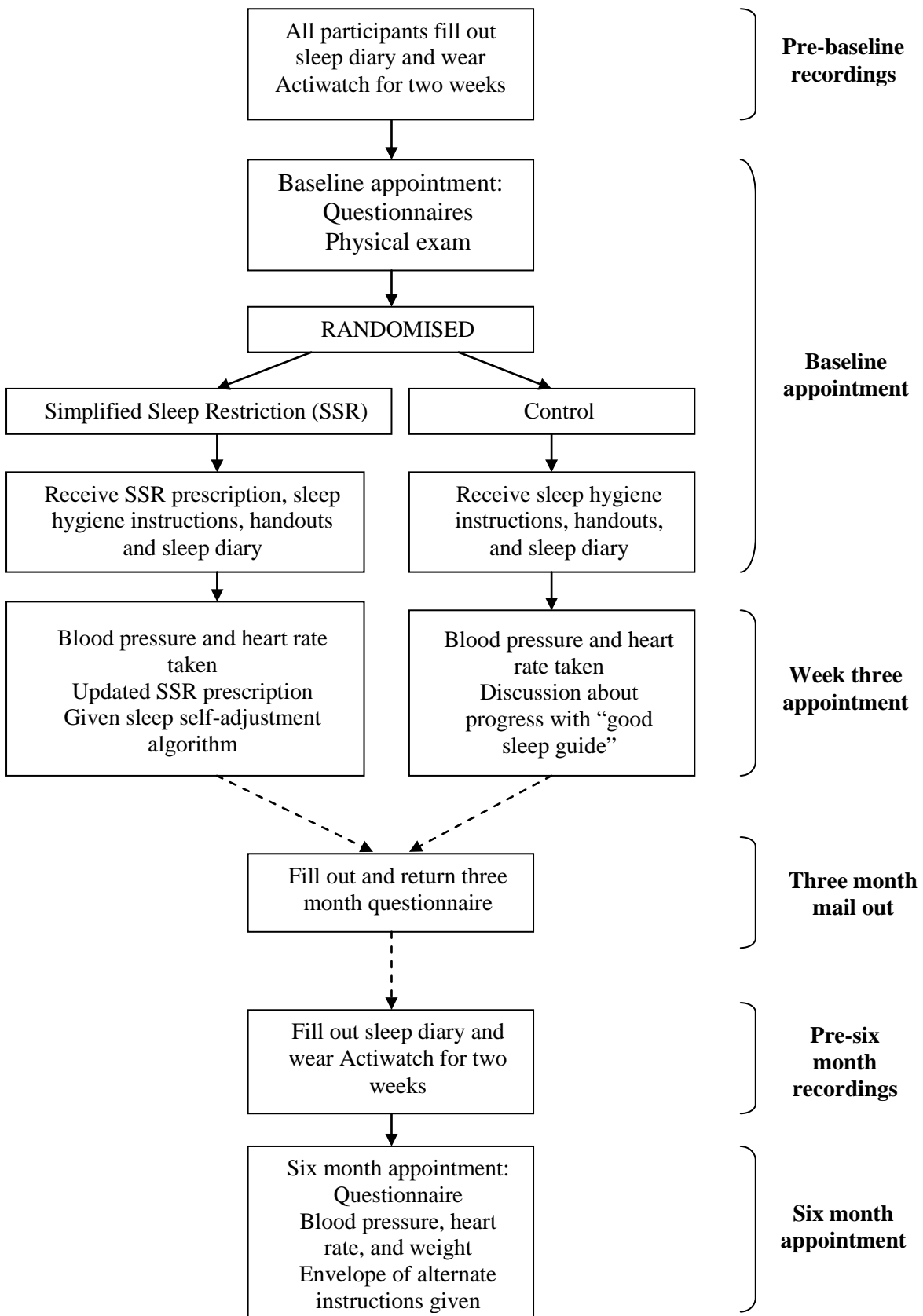


Figure 3-2: Participant flow through study protocol and assessments in the ReFRreSH trial

### **3.5.1 Simplified sleep restriction group**

#### **Rationale for sleep restriction**

Sleep restriction consolidates fragmented sleep by initially reducing time allowed in bed (the sleep opportunity). The resultant mild sleep deprivation enhances the endogenous sleep drive. This helps to promote continuous sleep while in bed. If the person feels sleepy throughout the day, the time allowed in bed is then systematically extended once continuous sleep has been established (defined qualitatively by the patient). If waking throughout the night starts to recur or if falling asleep becomes a problem, then the time in bed is restricted again until continuous sleep is re-established. The final time in bed is the time that is adequate to feel rejuvenated, while minimising periods of wakefulness throughout the night (or broken sleep).

Previous protocols have used sleep efficiency (total sleep time/time in bed) calculated from sleep diary data to inform adjustments prescribed by the health professional (L. Friedman, Bliwise, Yesavage, & Salom, 1991; Glovinsky & Spielman, 1991). In a more recently reported trial, the intervention adjustments to the participant's prescription were based on sleep latency and wakefulness averaged from the sleep diary (Buysse et al., 2011). The prescription was increased by 15 minutes if both sleep latency and wakefulness were less than 30 minutes, decreased by 15 minutes if both sleep latency and wakefulness were greater than 30 minutes, and time in bed was otherwise stayed constant. This algorithm was repeated weekly for the four weeks of the trial. The method used in the ReFRReSH trial allows the participants to make their own adjustments to the bedtime allowance based on their subjective assessment of sleep quality after they have had an initial four weeks of researcher-prescribed instructions by following a simple flowchart (see Figure 3-3). Sleep diary information is not required for these self-adjustments. This novel modification may make the sleep restriction protocol more suitable for use in the primary care setting without the need for repeated contact with healthcare providers.

Traditional sleep restriction procedures have involved immediate restriction of bedtime allowance to the actual hours spent asleep (L. Friedman et al., 1991; Morin, 2005; Morin, Bootzin, et al., 2006; Morin & Espie, 2003; M.T. Smith, Smith, Nowakowski, & Perlis, 2003; Spielman, Saskin, et al., 1987). The protocol used in this trial allows for an initial 50% reduction in the excess awake hours spent in bed. For example, if nine hours are spent in bed, with time spent asleep amounting to six of these hours, then there are three excess awake hours. Reducing the excess awake hours by 50% ( $3 \times 50\% = 1.5$  hours) therefore means instructing the participant to adjust their bedtime to 1.5 hours later than usual (if out-of-bed time in the morning remains constant). This milder initial restriction was recently described by Spielman (Glovinsky & Spielman, 2006), who had also conducted the first sleep



restriction trial published in 1987 (Spielman, Saskin, et al., 1987). The modification is an acknowledgement of the compliance issues that can be associated with an abrupt large reduction of time allowed in bed (L. Friedman et al., 1991).

### **The “sleep prescription”**

The initial time allowed in bed for each participant was calculated using the average time spent asleep per night according to sleep diary information. Prescription of “into bed” and “out of bed” times were negotiated with the participant. Simplified sleep restriction instructions were delivered by the health professional (the author) according to a standardised script (see Appendix S). Personalised instruction sheets were given to each participant in this group regarding negotiated bed times and out of bed times (Appendix T).

The prescribed sleep schedule was kept consistent for two weeks during which time a sleep diary was kept. After a two week period, reassessment of the sleep diary information enabled a revised sleep efficiency to be calculated and an updated sleep schedule prescription to be given (Appendix U). There were three possible sleep schedule prescriptions given at this appointment which are summarised below in Table 3-4.

*Table 3-4: ReFRReSH Trial Instructions for Adjustment of Sleep Schedules Based on Sleep in the Prior Fortnight*

| <b>Sleep quality</b>                                     | <b>Description</b>   | <b>Action</b>  |
|--|--|--|
| ▪ Poor quality or partially improved                     | Sleep efficiency <85% and subject not happy with their sleep         | Further restriction of time allowed in bed was made so that time in bed approximated time spent asleep plus 30 minutes (that is, a close match between sleep duration and time spent in bed). If sleep diary information was inadequate to quantify this, or if the instruction was met with resistance by the participant, the time allowed in bed was restricted by only 30 minutes further. |
| ▪ Improved   | Sleep efficiency $\geq$ 85% and daytime function not impaired        | No change to sleep prescription  |
| ▪ Either poor quality or improved but daytime impairment | Excessive daytime sleepiness or other significant daytime impairment | Thirty minutes added to the time allowed in bed  |

As well as receiving an updated bedtime prescription at the two week follow up appointment, participants were instructed how to use a “Sleep Self-Adjustment Algorithm” to self-manage their sleep schedule from week five onwards (Figure 3-3). The sleep self-adjustment algorithm enabled the participant to reassess their own sleep quality (a subjective overall impression for the preceding two weeks) and define their new bedtime “prescription” every two weeks. Consistent with previous research and in line with clinical convention (A. Fernando, personal communication, 2008<sup>4</sup>), the minimum time in bed allowance was five hours (Glovinsky & Spielman, 2006; Morin & Espie, 2003). The reason for defining this minimum time in bed allowance is three-fold. First, insomnia patients often misperceive the amount of sleep they are achieving each night leading to an underestimation of total sleep time. Secondly, the goal of sleep restriction protocol is not to create significant sleep deprivation, although a mild sleep deprivation may ensue for the first week or more, when the treatment is novel. Lastly, the five hour minimum prescription acts as a safety net against excessive daytime sleepiness. If sleep diary information was poor (for example, consistently reporting being awake all night, or being unsure if asleep or awake) the initial restriction of time allowed in bed was six hours to avoid inadvertently severely restricting the sleep of someone who had a poor perception of their true sleep.

The importance of consistently adhering to the prescribed bedtimes each night was emphasised to participants. Where possible, morning waking time was kept constant with any necessary adjustments made to the bedtime. If requested by the participant, a weekend sleep-in of one hour maximum was allowed in an effort to enhance compliance. This concession was based on the assumption that time-limited leeway in the weekend protocol would buffer against the mentality of “giving up” when faced with the lure of a weekend lie in, and a short “sleep-in” was unlikely to significantly impact upon the night time sleep schedule. There was some inbuilt scope for negotiation with the participant over the bedtime prescription. The rationale for this was two-fold: some flexibility was likely to enhance compliance and this also reflected the general practice consultation where a “patient-centered” approach allows patient input and preference to be considered in management plans (Bardes, 2012). Participants were given the opportunity to ask questions or to clarify instructions.

### **The sleep self-adjustment algorithm**

The sleep self-adjustment algorithm evolved from a desire to provide a pragmatic approach to sleep restriction that could easily be translated into everyday practice. The algorithm uses the traditional principles of sleep restriction (Spielman, Saskin, et al., 1987) and is based upon the method used in everyday practice by the research advisor (A. Fernando, personal communication). The intention was to simplify instructions by avoiding the need for ongoing sleep diary recordings or calculations by the

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<sup>4</sup> Psychiatrist and insomnia specialist

patients. Sleep restriction, in essence, is a simple principle which participants were being taught to use themselves to modify their sleep habits and regain control over their sleep.

The algorithm begins with a subjective assessment of the sleep experience over the preceding fortnight. Possible responses were that sleep had improved, that there was no change in sleep, or that sleep was worse than previously experienced. Contingent on this self-assessment the algorithm specified either an adjustment of +/- 30 minutes or no change to sleep times. As before, the revised nightly sleep prescription was adhered to for two weeks before further self-assessment by the participant. Participants were advised to mark their fortnightly sleep “check-in” on the calendar as a reminder.

### **Tailoring of the intervention**

It has been previously noted that participants were advised a maximum sleep in of one hour on the weekend was allowable if absolutely necessary; however this was discouraged as it may reduce the treatment effect. If participants wanted to use sleep medication they were advised that regular use was not permissible on the trial as this would confound or dilute any treatment effect of the intervention. However, occasional use - as opposed to regular intermittent use - was permitted as long as this was no more than a few times per month and that this use was recorded. If participants queried the instruction of only using the bed for sleep, where they had previously enjoyed the routine of reading in bed and wanted to continue with this the following instructions were given: the less reading in bed the better and if reading must be done in bed, to limit this strictly to 10 to 15 minutes maximum. Participants were encouraged to keep wake up times constant to “anchor” their sleep pattern. However, some flexibility was permitted to make the sleep period more acceptable on an individual basis.

### **Standardisation of the intervention**

The sleep restriction instructions were administered using a standardised script (Appendices S and U). Time taken to deliver the instructions was recorded using a stopwatch. Those in the simplified sleep restriction group received the control group instructions at the end of their six month involvement in the trial once data collection was complete.

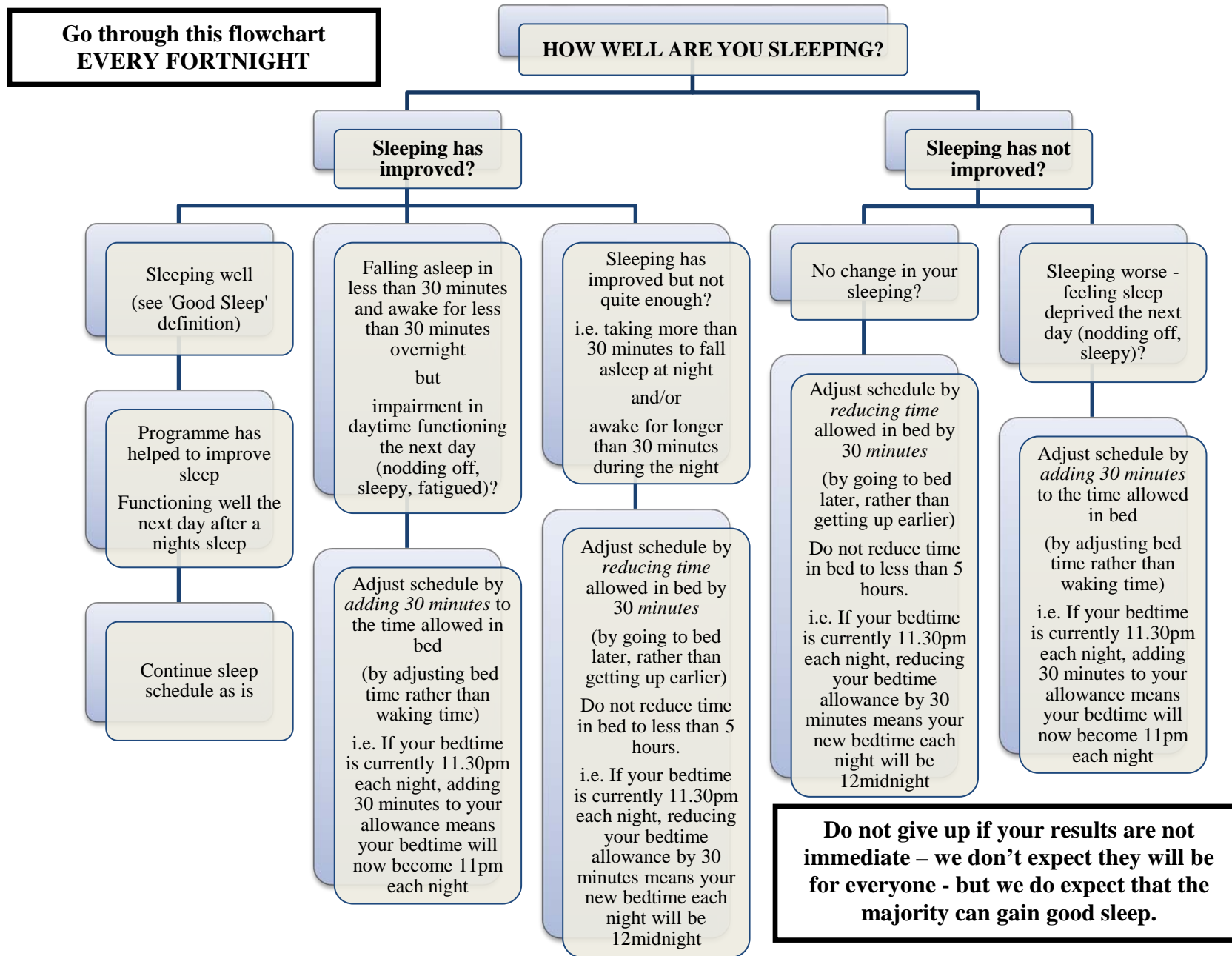


Figure 3-3: ReFRoSH trial “Simplified Sleep Restriction” intervention sleep self-adjustment algorithm

### **3.5.2 Control group**

The control group received basic instructions regarding good sleep habits, which were described verbally and included in a handout which was used as a script (Appendix P). The “good sleep guide” instructions consisted of information such as avoiding caffeine, relaxing before bedtime and creating a sleep-conducive pre-bed routine. It avoided including any instructions to do with sleep schedule and naps (and thus is different to a traditional sleep hygiene intervention), which have been found to have some effect on sleep (Lacks & Rotert, 1986), in order to provide a control that did not include specific sleep pattern advice. The control group was seen at the same time points as the intervention group (Figure 3-2). The aim of this method was to match the contact “intensity” and contact time with investigators to that received by the simplified sleep restriction group. The control group were offered the simplified sleep restriction intervention at the end of their six month involvement in the trial once data collection was complete (see Appendix V).

### 3.6 Outcome Measures

The outcomes measured and time points for assessment are presented in Table 3-5 with description of each measure in the section below.

*Table 3-5: Outcome Measures for the ReFReSH Trial and Time Points for Assessment*

| Measure                                     | Assessment time point |              |            |
|---|-----------------------|--------------|------------|
|   | Baseline              | Three months | Six months |
| Primary outcome                             |                       |              |            |
| Pittsburgh Sleep Quality Index <sup>a</sup> | X                     | X            | X          |
| Insomnia Severity Index <sup>b</sup>        | X                     | X            | X          |
| Sleep diary sleep efficiency (%)            | X                     |              | X          |
| Actigraphy sleep efficiency (%)             | X                     |              | X          |
| Secondary outcomes - sleep                  |                       |              |            |
| Epworth Sleepiness Scale <sup>c</sup>       | X                     |              | X          |
| Flinders Fatigue Scale <sup>d</sup>         | X                     |              | X          |
| Sleep measures (SOL, WASO, TST)             | X                     |              | X          |
| Secondary Outcomes – mental health          |                       |              |            |
| Depression <sup>e</sup>                     | X                     |              | X          |
| Anxiety <sup>f</sup>                        | X                     |              | X          |
| Harms                                       |                       |              |            |
| Adverse events                              | X                     |              | X          |
| Physiological measures <sup>g</sup>         | X                     |              | X          |

*Note.* Abbreviations: SOL = sleep-onset latency, WASO = wake after sleep onset, TST = total sleep time. <sup>a</sup>(Buysse et al., 1989). <sup>b</sup>(Bastien et al., 2001). <sup>c</sup>(Johns, 1991). <sup>d</sup>(Grasidar et al., 2007). <sup>e</sup>PHQ-9 (Kroenke et al., 2001). <sup>f</sup>GAD-7 (R.L. Spitzer et al., 2006). <sup>g</sup>Blood pressure (BP), heart rate (HR) and weight measured at baseline and six months, BP and HR at week three.

### **3.6.1 Primary outcomes**

The primary outcome for the study was sleep quality. Sleep quality was assessed both subjectively and objectively. Subjective sleep quality was assessed using the Insomnia Severity Index (Bastien et al., 2001) and the Pittsburgh Sleep Quality Index (Buysse et al., 1989). Objective sleep quality was assessed using sleep efficiency ( $[\text{total sleep time}/\text{time in bed}] \times 100\%$ ) calculated from both sleep diary and actigraphy.

### **3.6.2 Secondary outcomes**

The secondary outcome measures included both sleep-related measures and mental health measures. The sleep-related measures were sleepiness assessed using the Epworth Sleepiness Scale (ESS) (Johns, 1991); fatigue assessed using the Flinders Fatigue Scale (FFS) (Grasidar et al., 2007); and the sleep parameters of sleep-onset latency, wake after sleep onset and total sleep time. The sleep parameters were measured using both sleep diary and actigraphy. The mental health measures were depression assessed using the PHQ-9 (Kroenke et al., 2001); and anxiety was assessed using the GAD-7 (Kroenke et al., 2007; R.L. Spitzer et al., 2006).

The sleep parameters used have been identified as the most useful combination of actigraphic parameters to assess insomnia (Natale, Plazzi, & Martoni, 2009). However, the number of awakenings overnight was not used as an outcome measure although this has been suggested as a useful measure (Buysse et al., 2006; Natale et al., 2009). An attempt was made to balance the statistical need for limited outcome measures with the outcome measures that have been recommended. If all recommended outcomes had been included this would have increased the risk of a type 1 error, where a significant difference is found due to chance because of multiple comparisons, leading to an incorrect rejection of the null hypothesis (Feise, 2002).

The outcome measures chosen reflect the 2006 expert panel consensus recommendations for a standard research assessment of insomnia (Buysse et al., 2006). However, minor modifications were made to these measures for the primary care environment, although actual validated measurement tools were not modified. Consensus recommendations suggest the assessment of fatigue using the Multidimensional Fatigue Inventory (Smets, Garssen, Bonke, & De Haes, 1995) or the Fatigue Severity Scale (Krupp et al., 1989). However the author chose to use a relatively new measure - the Flinders Fatigue Scale (Grasidar et al., 2007). This scale has been shown to be a valid and reliable brief measure of fatigue in those with insomnia and has been evaluated in the context of those with insomnia undergoing treatment (Grasidar et al., 2007). Whereas the consensus recommendations suggest assessing mood using the Inventory of Depressive Symptomatology (Rush, Gullion, Basco, Jarrett, & Trivedi, 1996) or the Beck Depression inventory II (Beck, Steer, & Brown, 1996) for depression and the State-Trait Anxiety Inventory

(Spielberger C.D., Gorsuch R.C., & Lushene R.E., 1970) for anxiety, these have been replaced with the PHQ-9 (Kroenke et al., 2001) measuring depression and the GAD-7 measuring anxiety (Kroenke et al., 2007; R.L. Spitzer et al., 2006) in the current study. Both the PHQ-9 and the GAD-7 are brief measures that have been validated in the primary care setting making them more appropriate for this study population and very quick to administer (Kroenke et al., 2001; R.L. Spitzer et al., 2006). The consensus recommendations for the standard research assessment of insomnia also suggest using the SF-36 scale to measure quality of life (Buysse et al., 2006; Ware & Sherbourne, 1992). This was not undertaken in the present study as it was not considered a priority outcome in assessing the effectiveness of sleep restriction and the author was concerned about multiple outcomes, as well as the participant burden of research measures. It was important that the assessment was not overly onerous for the participants both in terms of compliance and in avoiding undue “research treatment effect” by the extensive filling out of questionnaires.

### **3.7 Randomisation**

“Sound scientific clinical investigation almost always demands that a control group be used against which the new intervention can be compared”(L Friedman, Furberg, & DeMets, 2010, p. 68). Randomisation is a critical aspect of clinical trial design and is “the preferred way of assigning participants to control and intervention groups” (L Friedman et al., 2010; Schulz, Altman, & Moher, 2010, p. 68). Successfully implemented, randomisation eliminates selection bias, produces comparable groups (both measured and unknown prognostic factors), and confers validity to statistical tests of significance (L Friedman et al., 2010). Without randomisation, it would be possible that participants of a particular kind were selected (consciously or unconsciously) to have a particular treatment (for example, more highly motivated or those with more severe insomnia might be selected to be in the sleep restriction group) (CONSORT group, 2013). The resulting selection bias may then lead to inaccurate conclusions about a treatment’s effect (Hartling et al., 2009). The randomisation procedure for the ReFRReSH trial is described below.

#### **3.7.1 Sequence generation**

Randomisation of participants was performed using a computer-generated block randomisation scheme by a statistician not involved in patient recruitment or assessment, using SAS software, version 9.2 (SAS Institute Inc., Cary, NC, USA). A block size of six was used. This was based on the assumption that a minimum of six participants would be recruited from each practice. Block randomisation ensures that there is balance between the groups throughout recruitment (L Friedman et al., 2010). With a block size of six,



randomisation is balanced after every six participants are recruited, therefore ensuring randomisation within each practice would be balanced. This would then serve to minimise any systemic sampling errors (L Friedman et al., 2010). For example, if a particular practice had patients of a certain characteristic (e.g. highly motivated) and all of those participants happened to receive the intervention because there was no block randomisation, the effect of the intervention might be overestimated. Using a block randomisation scheme also meant that if the trial was terminated early the randomisation would be balanced (L Friedman et al., 2010).

### **3.7.2 Allocation concealment and implementation**

A central telephone system was used to implement the random allocation sequence following enrolment and baseline assessment. At the baseline appointment, after all data were collected, the participant's unique code was texted in real time by the author to the central administrator who texted the next group allocation according to the randomisation sequence. The administrator had no direct contact with study participants and was not aware of the interventions being delivered. The random allocation sequence was concealed until interventions were assigned.

### **3.8 Blinding**

Because of the nature of the intervention it was not possible to blind the author who also administered the intervention instructions. However, the author was blind to allocation when assessing baseline measures. Furthermore, the participants were informed they would be allocated one of two simple, non-drug treatments for insomnia and were thus blind to the exact nature of the intervention content prior to randomisation. Interventions were delivered using standardised scripts to minimise bias. Almost half (41%) of the outcome measures were assessed by a research assistant blinded to group allocation. Where a research assistant was not available to perform the outcome assessments the author assessed outcomes by collecting completed questionnaires and taking the blood pressure, pulse, and weight recordings. In this situation the participants were asked to countersign each measurement to ensure data accuracy (the blood pressure machine and scales had a digital display). The outcomes questionnaires involved quantitative data to reduce reporting bias. Data were double-entered by the author and a research assistant who was blind to group allocation. The two versions were compared electronically and any differences were resolved by referencing the original questionnaire or recording. The outcome sleep diaries and actigraphy were analysed by the researcher. A random sample of 20% of the participants had two weeks of sleep diary data analysed by a blinded research assistant (Ka Eng Soh, KS) to check the accuracy. Another random sample

of 20% of the participants had two weeks of actigraphy (either baseline or six month recordings) analysed by a blinded research assistant familiar with actigraphy analysis (Anisoara Jardim, AJ).

### **3.9 Sample Size Calculations**

The sample size was calculated on the basis of data ( $n = 45$ ) from a pilot trial looking at the effectiveness of a brief version of bedtime restriction (sleep restriction) (Fernando et al., 2013). The study population was those with primary insomnia recruited from the community via newspaper advertisement (the treatment was not advertised). Sleep quality was measured using the question of “how would you rate your sleep?” with the possible responses being: “much better”, “better”, “same”, “worse”, or “much worse”. The responses were divided into “improved sleep” (much better, better) or “no improvement” (same, worse, much worse) to create the binary outcome. The results of this six week study showed the absolute benefit from the treatment was 38% (95% confidence interval 8.8% to 59%) with 73% in the bedtime restriction group experiencing improved sleep compared with 35% in the control group.

To detect a difference of 30% ( $\alpha = 0.05$ , 80% power) 45 participants per group were required. The sample size for this trial was therefore 100 to allow for 10% attrition. We also estimated the number required to show a 25% difference as statistically significant, which would have required 132 participants ( $\alpha=0.05$ , 80% power). Although the initial aim was to recruit this number, we reverted to our lower estimate when the recruitment rate proved a lot slower than expected. However, both sample size calculations had been carried out prior to the trial starting (Appendix W).

### **3.10 Analysis**

Most of the data entry and data cleaning was carried out by the author. Baseline descriptive analyses were undertaken by the author using Excel and SPSS (version 21). The difference between the groups at follow-up in the primary and secondary outcomes was analysed using regression models in SAS software, version 9.3 (SAS Institute Inc., Cary, NC, USA) by Arier Chi Lun Lee (ACLL, biostatistician in the Department of Biostatistics, Department of Population Health, The University of Auckland) in consultation with the author. Final outcome graphs and tables were constructed by the author.

Mixed models for repeated measures were used for outcomes (PSQI and ISI) with two post-baseline time points (three months and six months) (Brown & Prescott, 1999; Verbeke & Molenberghs, 2000) (SAS

MIXED procedure (Littell, 2006)). Multiple linear regression was used to analyse all other outcomes which had only one post-baseline time point (six months). All available data were used and adjusted for age, sex, and baseline insomnia severity (ISI score).

The definition of “categorical treatment outcome” described by Buysse et al. (2011) was used to determine treatment response, remission, partial response, or non-response (Table 3-6). These four categorical outcomes were then collapsed into two categories: remission or response versus partial response or non-response. The absolute risk reduction, number needed to treat (NNT) and 95% confidence intervals were calculated using unadjusted data. The four and two category outcomes were then analysed using ordinal and logistic regression, respectively, adjusted for age, sex and baseline insomnia severity. From this modelling, adjusted odds ratios and 95% confidence intervals were obtained.

*Table 3-6: Definition of Insomnia Categorical Treatment Outcomes*

| <b>Treatment outcome</b> | <b>Definition</b>   |
|--------------------------|---|
| ▪ Response               | Reduction in PSQI <sup>a</sup> score $\geq 3$ points <i>or</i> improvement in SE <sup>b</sup> of $\geq 10\%$  |
| ▪ Remission              | Response criterion <i>and</i> final PSQI <sup>a</sup> score $\leq 5$ <i>and</i> SE <sup>b</sup> $\geq 85\%$   |
| ▪ Partial response       | Reduction in PSQI <sup>a</sup> score $\geq 3$ points <i>or</i> improvement in SE <sup>b</sup> of $\geq 10\%$<br><i>But</i> worsening on the other measure/s |
| ▪ Non-response           | Reduction in PSQI <sup>a</sup> score $< 3$ points <i>and</i> increase in SE <sup>b</sup> $< 10\%$   |

*Note.* Categorical treatment outcomes based on those defined by Buysse et al. (Buysse et al., 2011). <sup>a</sup>Pittsburgh Sleep Quality Index (Buysse et al., 1989) <sup>b</sup>Sleep efficiency calculated from sleep diary (TST/TIB x 100%)

No missing data imputation was performed. All analyses used an intention to treat approach. An intention to treat analysis involves analysis of all randomised participants in the groups to which they were randomly assigned (Hollis & Campbell, 1999). Using this approach, participants were analysed in the groups to which they were randomly assigned regardless of their adherence to the treatment, the treatment they actually received, if they were subsequently found to be ineligible for inclusion, or if they subsequently dropped out of the intervention (Fergusson, Aaron, Guyatt, & Hebert, 2002). The intention to

treat method is suggested to be the most conservative approach to analysis, thus minimising the chance of type 1 error (finding a difference when one does not exist) (Fergusson et al., 2002).

### **Additional analyses**

#### ***Sensitivity analysis***

Critics have suggested that an intention to treat analysis can be vulnerable to type II error (incorrectly accepting that there is no difference between the groups) (Fergusson et al., 2002). Therefore, sensitivity analysis was performed using a “complete case” analysis whereby any participant with missing data was excluded from the analysis to observe if this substantially changed the outcomes. Complete case sensitivity analysis was carried out for the PSQI and ISI scores.

#### ***Hypnotic use***

A sensitivity analysis adjusting for hypnotic use at six months was performed to determine if this had any significant effect on the results. Hypnotic use at six months was assessed using the “medication use” component score of the PSQI (no use, less than once a week, once or twice a week, three or more times a week) and entered as a covariate in the outcome modelling for the primary outcomes. Although it is not ideal to use hypnotic use derived from the PSQI, this was the only information available regarding hypnotic use.

#### ***Adverse effects***

Statistical testing was not performed to compare the occurrence of adverse events between groups due to the small number of events recorded. However, a senior biostatistician (AS) acted as a data monitor and assessed rates of adverse events at three weeks and final follow-up data collection to ensure there were not worrying trends in differences of adverse events.

#### ***Physiologic measures***

For the physiologic measures of blood pressure, heart rate, and body mass index the difference between the observed mean scores within groups pre and post treatment was compared.

### **3.10.2 Minimising confounding**

Confounding is “a difference between treatment groups in the characteristics that influence the association between the treatment and outcome measures” (Sedwick, 2012, p. e7951). It is important to control for confounding variables as failure to do so may undermine the validity of the trial results. Age and sex are factors known to influence sleep quality as there is an increased prevalence of insomnia in females and older adults (Ohayon, 2002). Therefore, if one of the treatment groups had greater numbers of older adults

or females by chance, the response to sleep restriction may have been more dramatic, or less evident (if being older or female causes a more refractory type of insomnia). Insomnia severity at baseline was also hypothesised to be a potential factor that influences sleep quality at outcome. For example, it may be that those with a more severe insomnia at baseline have a more dramatic response to sleep restriction, or the converse situation may apply where those with a more severe insomnia at baseline are not going to improve with any treatment given. Randomisation is a way to address confounding at the trial design stage. As previously mentioned, the treatment groups in this trial were randomly allocated (Section 3.7). Randomisation helps to minimise confounding but does not eliminate it entirely, especially if the trial has a small sample size or if dropouts mean that at analysis the treatment groups have become unbalanced with respect to their baseline characteristics, which could bias results. Therefore, along with randomisation, adjusting for potential confounding factors was achieved by incorporating gender, age, and baseline ISI into the statistical model. There were a large number of practices involved in recruitment and the practices were not involved in delivering the intervention. Therefore, the statistical model was not adjusted for “practice” effect although this was considered.

### **3.11 Materials and Measures**

The methods of recording the sleep parameters used in the trial were actigraphy (objective) and sleep diary (subjective) and these are described below. Validated questionnaires were used to quantify sleep quality, sleepiness, fatigue, depression, and anxiety. Physiological measures of blood pressure, heart rate and body mass index were recorded as part of the monitoring of adverse effects. The description, validity and reliability of these measures are described below.

#### **3.11.1 Sleep measures**

##### **Sleep diary**

The sleep diary is a daily recording of nightly sleep patterns. Participants were asked to fill out the diary first thing in the morning for the preceding night’s sleep. The diary recorded naps, time of getting into bed, time of turning out the lights (with the intention of sleep), time taken to fall asleep, number of overnight awakenings, duration of each awakening, time of final awakening, time of getting out of bed for the day and any time the Actiwatch was removed (Appendix M). Participants were asked to estimate these times. For example, checking the clock overnight to determine the timing and duration of overnight awakenings

was not required. Participants were instructed to fill out a daily sleep diary for a two-week period prior to the baseline and six month outcome measurements.

The sleep diary used in the trial was designed by the author based on the design used by Morin (Morin, 1993). Use of the sleep diary was explained to the participants using instructions used by Morin with his permission (Appendix M).

### ***Validity and reliability***

Sleep diaries are considered to provide a valid and reliable relative index of sleep disturbance (Coates et al., 1982). They are useful for identifying general trends in sleep patterns and may also be helpful in ruling out possible circadian rhythm disorders (Buysse et al., 2006) although they were not used for this latter purpose in the ReFRReSH trial. The sleep diary information also ensured the study inclusion criteria for insomnia was met (sleep-onset latency greater than 30 minutes and/or greater than 30 minutes of wake after sleep onset, occurring on at least three nights per week). Whilst those with insomnia appear to underestimate total sleep time and overestimate sleep-onset latency and wake after sleep onset compared to normal sleepers any estimation error appears to stay consistent over time (Coates et al., 1982; Means, Edinger, Glenn, & Fins, 2003). Therefore, sleep diary estimates of sleep parameters are able to provide a reasonable gauge of change over time (Means et al., 2003). The sleep diary also has the advantage over other methods of assessing sleep such as polysomnography by being more likely to capture the night-to-night variability that is often seen in chronic insomnia (as compared with one or two nights of polysomnography data collection) (Buysse et al., 2006). Fourteen nights has been recommended as a reasonable sampling period (Buysse et al., 2006; Wohlgemuth, Edinger, Fins, & Sullivan, 1999).

### ***Use***

The sleep diary allowed collection of the following variables: overall time in bed (“Overall TIB”), time in bed (“TIB”), total sleep time (“TST”), sleep-onset latency (“SOL”), wake time after sleep onset (“WASO”), and sleep efficiency (“SE”). According to the standard definitions of sleep parameters (Table 3-7), TIB refers to the time in bed starting from the moment of turning off the lights with the intention of sleeping. In line with standard research protocol, TIB was used to calculate sleep efficiency (Buysse et al., 2006). An additional sleep diary parameter was used in this trial, termed by the author as overall TIB. This value reflected the time spent in bed from the time of getting into bed until the time of getting out of bed to start the day. This value was used to calculate the “bedtime efficiency” (TST/Overall TIB) which was used when prescribing a sleep schedule for the participant. This value was used (rather than the standard definition of sleep efficiency) in order to reflect that in some people with insomnia there is a long period of

wakefulness in bed before turning out the lights to sleep, as well as periods of wakefulness in bed after turning out the lights. For example, it is common for people with insomnia to go to bed early to try and catch more “opportunity” for sleep. However, they are often getting into bed when they are not yet ready for sleep and may spend long periods reading or watching television. This excess time in bed awake needs to be taken into account when prescribing a sleep schedule in order to match time in bed with time actually spent sleeping. It would not be taken into account if the standard TIB value was used to determine the sleep prescription. However, when reporting trial results, the standard definition of sleep efficiency (TST/TIB x 100%) was used for both sleep diary data and actigraphy data as per research convention (Buysse et al., 2006).

The sleep diaries were analysed using a protocol developed for this study by the author, which provided standardised instructions to deal with aberrant entries; for example, where values were missing, unusual events occurred during the night, or annotations were used instead of numerical values by the participant filling out the diary (Appendix X).

*Table 3-7: Standard Definition of Sleep Parameters*

| <b>Sleep parameter</b>        | <b>Abbreviation</b> | <b>Definition (Buysse et al., 2006)</b>  |
|-------------------------------|---------------------|--|
| Time in bed                   | TIB                 | Time in bed, starting from the moment of intention to fall asleep and finishing on final arising |
| Sleep-onset latency           | SOL                 | The time it takes to fall asleep starting from the moment of intention to fall asleep            |
| Wake after sleep onset        | WASO                | Total amount of time awake during the night, excluding SOL and TWAK                              |
| Terminal wakefulness          | TWAK                | Amount of time awake between the final awakening and time of getting out of bed                  |
| Total sleep time              | TST                 | Actual time slept. Calculated from sleep diary as TST=TIB-SOL-WASO-TWAK                          |
| Sleep efficiency (percentage) | SE                  | Percent of time spent in bed asleep. When using sleep dairies, calculated as TST/TIB x 100       |

## **Actigraphy**

Wrist actigraphy was used in conjunction with the sleep diary recordings to offer an objective measurement of sleep parameters. Wrist actigraphy uses a battery-powered activity-monitoring device of similar appearance to a wristwatch. All actigraphy devices in this trial were Actiwatch-64® (Mini-Mitter Co.,Inc/Respironics Inc, Bend, Oregon). The Actiwatch was worn by the participant on their non-dominant wrist for a two week period at baseline (immediately prior to baseline appointment) and at six months. The watch was worn continuously except for times of water immersion such as bathing. Every Actiwatch had a unique serial number and each participant wore the same device for both recordings to minimise the risk of error.

Wrist actigraphy utilizes a multidirectional piezoelectric accelerometer to monitor the degree and intensity of a patient's motion (Mini Mitter Co., 2004). Its use is based on the principle that there is reduced movement during sleep and increased movement when awake (M. Littner et al., 2003). The Actiwatch accelerometer sampling frequency was 32Hz, with a sensitivity of 0.05g-force and filter bandwidth of 3-11Hz (Mini Mitter, 2006). The device detects motion, which is then transduced into an electrical current, digitized and stored as an activity "count" (Mini Mitter, 2006).

Data were stored in the Actiwatch until the Actiwatch was collected from the participant. Data were then downloaded using the ActiReader® box, which used a serial port interface with the research laptop computer and the Actiware-5.70.1® software (Mini-Mitter Co.,Inc, Bend, Oregon). Downloaded data were presented as an actigram – a graphic view of the rest/activity history of the subject. The "rest" interval was set using data obtained from the accompanying sleep diary ("what time did you turn the lights out?" and "what time did you get up for the day?"). The setting of the rest interval was in line with current research convention.

The software scored all epochs as either sleep or wake. This categorisation was determined by comparing activity counts for the epoch and those immediately surrounding it with a threshold value set by the researcher (Mini Mitter, 2006). The wake threshold was set at medium, with a wake threshold value of 40 activity counts for the sampling epoch. If the number of activity counts exceeded the set threshold, the epoch was scored as wake by the software algorithm (Mini Mitter, 2006). Conversely, if the number of activity counts is equal to, or below, the set threshold, the epoch was scored as sleep (Mini Mitter, 2006). The Actiwatch was calibrated to record 30 second epochs - the standard sampling interval for insomnia research (Lichstein et al., 2006; Mullaney, Kripke, & Messin, 1980)). The software algorithm enabled summary statistics of the sleep parameters SE, SOL, WASO, and TST to be determined.



### ***Validity and reliability***

Actigraphy is useful in the assessment of insomnia, sleep variability assessment, and measurement of treatment effects (Buysse et al., 2006; M. Littner et al., 2003; Vallieres, Morin, Vallieres, & Morin, 2003). It has the advantage of assessing sleep over multiple nights and is a cheaper and more convenient alternative to overnight polysomnography (which is no longer considered to be the “gold-standard” quantitative measure of insomnia against which all other measures are judged (Buysse et al., 2006)). Actigraphy has been shown to be able to differentiate between normal sleepers and those with insomnia (Natale et al., 2009). Actigraphy has been validated in those with insomnia using the Actiwatch-64® and associated software proving to be a satisfactory objective measure of WASO, TST and SE (Brooks, Friedman, Bliwise, & Yesavage, 1993; Lichstein et al., 2006). The use of actigraphy for evaluating response to treatment for patients with insomnia has been endorsed by recent practice parameters recommendations (Morgenthaler, Alessi, Friedman, & al, 2007).

The baseline recording and sleep diary analysis were performed prior to randomisation. Actiwatch-64® recording data were retrieved and analysed after the treatment or control instructions were given. The software programme used was Respironics Actiware version 5.70.1® software (Mini-Mitter Co.,Inc, Bend, Oregon). The actigraphic data recorded prior to the baseline and six month appointments were analysed by the author and therefore was an unblinded analysis. However, a random selection of 20% of the participants had a two week period of actigraphy (baseline or six month) double read by a blinded independent observer (AJ) who was familiar with the use of actigraphy and the Actiware® software to ensure accuracy. The actigraphy analysis protocol can be seen in Appendix Y.

Actigraphy data were analysed in two ways. Initially, sleep diary data were entered using the time of getting into bed as the start of the rest interval and the time of getting out of bed to start the day as the end point of the rest interval. The rest interval is used by the Actiware software algorithm to generate the sleep statistics. After consultation with others in the field of insomnia research, it was decided to re-enter sleep diary data into the Actiware program using the time the participant turned out the lights with the intention of sleeping as the start of the rest interval and the time of getting out of bed to start the day as the end point of the rest interval. This enabled the Actiware program to more accurately calculate the SOL time (Buysse et al., 2006) and is in keeping with the method used in a recent similar trial (Buysse et al., 2011).

### 3.11.2 Questionnaires

#### Sleep quality

##### *Pittsburgh Sleep Quality Index*

The Pittsburgh Sleep Quality Index (PSQI) is a self-completed questionnaire designed to assess sleep quality over a one month period (Buysse et al., 1989). It is comprised of seven components assessing: subjective sleep quality, sleep onset latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. Summary component scores are combined to yield an overall global score (range 0 - 21). A global score  $>5$  is able to differentiate between “good sleepers” and “poor sleepers” (diagnostic sensitivity 89.6% and specificity 86.5%, kappa = 0.75,  $p < 0.001$ ) (Buysse et al., 1989). Although this index was not specifically designed for insomnia, it has been commonly used in insomnia research and is a recommended measure for the standard research assessment of insomnia (Buysse et al., 2006; Morin, 2003). A three point reduction in the PSQI score has been suggested to represent a clinically meaningful improvement in those with primary insomnia (Buysse et al., 2011).

##### *Insomnia Severity Index*

The Insomnia Severity Index (ISI) is the other recommended measure for assessing global sleep and insomnia symptoms (Bastien et al., 2001; Buysse et al., 2006). It is a brief, self-report questionnaire assessing the patient’s perception of his or her insomnia. It comprises of seven questions assessing: the severity of current problems (onset, maintenance, early awakening), satisfaction with current sleep patterns, interference with daytime functioning, noticeability of impairment, and concern caused by the sleep problem. Each item is rated on a scale of 0 to 4 with a total score ranging from 0 to 28. Scoring guidelines for quantifying the insomnia severity have been suggested as: 0 to 7 (no significant insomnia), 8 to 14 (subthreshold insomnia), 15 to 21 (clinical insomnia - moderate), and 22 to 28 (clinical insomnia - severe) (Bastien et al., 2001). The ISI complements the PSQI in the assessment of sleep quality by the additional assessment of the degree of impairment and emotional distress caused by insomnia. The psychometric properties of the ISI have been evaluated in those with insomnia and it has been shown to be a reliable and valid instrument to quantify subjective insomnia severity (Bastien et al., 2001). It has also been shown to be a valid and sensitive measure to detect changes in perceived sleep difficulties with treatment (Bastien et al., 2001). A six point reduction in the ISI score has been recommended to represent a clinically meaningful improvement in those with primary insomnia (M. Yang, Morin, Schaefer, & Wallenstein, 2009).

## **Sleepiness**

### ***Epworth Sleepiness Scale***

The Epworth Sleepiness Scale (ESS) is a brief, self-administered questionnaire that provides a measurement of the subject's general level of daytime sleepiness (Johns, 1991). The ESS asks subjects to rate their level of sleepiness (would never doze = 0 to high chance of dozing = 3) over eight situations giving a summary score (0 - 24). The higher the summary score, the higher the level of daytime sleepiness, with scores above 16 indicating a high level of daytime sleepiness. The ESS has been shown to be a valid measure of sleepiness when compared with the Multiple Sleep Latency Test (MSLT) (the most commonly used objective test of sleepiness) and polysomnography (Carskadon & Dement, 1977; Richardson et al., 1978). In an early study, the ESS was tested in normal sleepers and in those with various diagnosed sleep disorders (Johns, 1991). The study showed that only those with moderate to severe obstructive sleep apnoea syndrome, narcolepsy or idiopathic hypersomnia scored above 16 (sleep disorders known to be associated with excessive daytime sleepiness). All those with narcolepsy or idiopathic hypersomnia scored above 10, as did those with severe obstructive sleep apnoea (except for one subject who had little clinical effects from his obstructive sleep apnoea (Johns, 1991)), and the insomnia subjects had low ESS scores ranging from 0-6. The questionnaire has also been shown to have good internal consistency (Cronbach's alpha = 0.88) and test-retest reliability (Johns, 1992).

Although the ESS is not a diagnostic tool, it was used as a screening tool in this study whereby those with a score >10 were excluded in the screening phase using the comprehensive sleep disorders questionnaire. The reason for exclusion of those with high levels of sleepiness was two-fold. Firstly, a higher ESS score may have indicated that obstructive sleep apnoea or another disorder other than primary insomnia may have been present. Secondly, as the study intervention involved potentially inducing a mild state of sleep deprivation any worsening of sleep deprivation in one who is already sleep deprived may well have raised additional safety concerns (for example drowsy driving). It is important to note that whilst sleepiness (representing the actual tendency or propensity to sleep (Buysse et al., 2006)) is not a feature commonly associated with those suffering from primary insomnia (Moul et al., 2002; Ohayon, 2002; Stepanski et al., 1988), when subjected to sleep deprivation those with primary insomnia exhibit expected increases in sleepiness (Stepanski et al., 2000). Thus, insomnia is not synonymous with sleep deprivation. The intention of the simplified sleep restriction protocol was to harness the sleep-inducing effect of mild sleep deprivation in those who were not already significantly sleep deprived (excessively sleepy).

## **Fatigue**

### ***Flinders Fatigue Scale***

Fatigue was measured using the Flinders Fatigue Scale (Grasidar et al., 2007). Fatigue is described as subjective feelings of weariness, tiredness, or exhaustion as opposed to feelings of sleepiness (which denotes an increased propensity to sleep or doze) (Johns, 1991; Shapiro et al., 2002). This scale was chosen as it is a brief scale designed for measuring daytime fatigue associated with insomnia. The Flinders Fatigue Scale (FFS) is a seven-item scale that measures various aspects of fatigue experienced over the preceding two weeks: how much of a problem, problem with everyday functioning, distress caused, frequency, times of the day fatigue is typically experienced, severity, and how much fatigue was caused by poor sleep. The six items are scored from 0 (not at all) to 4 (extremely/entirely). One item consists of a multiple item check-list for the times that fatigue is experienced throughout the day and is scored as a sum of the times checked. The total fatigue score ranges from 0 to a maximum 31, with higher scores indicating a greater level of fatigue (Grasidar et al., 2007).

As fatigue is one of the most frequent complaints of those with insomnia, a reduction in daytime fatigue is a clinically meaningful endpoint for assessment of an insomnia treatment (Morin, 2003). The FFS has been shown to be a brief, reliable and valid measure of fatigue (Grasidar et al., 2007). It was the first fatigue measure to be validated in insomnia patients undergoing treatment, and has been shown to be sensitive to the effects of cognitive behavioural therapy for insomnia (Grasidar et al., 2007). The FFS also shows good discriminant validity with the Epworth Sleepiness Scale, suggesting these scales measure different constructs (Grasidar et al., 2007; Johns, 1991).

## **Depression**

### ***PHQ-9***

The Patient Health Questionnaire-9 (PHQ-9) (Kroenke et al., 2001) is the 9-item depression module of the Patient Health Questionnaire (PHQ) (R. L. Spitzer, Kroenke, & Williams, 1999). The PHQ-9 is a self-report questionnaire designed for use in the primary care population. It consists of nine questions designed to correspond to the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)* diagnostic criteria for major depressive disorder (American Psychiatric Association, 1994). The questionnaire asks about symptoms experienced in the past two weeks. Items are rated according to the frequency of experiencing the specified symptom from 0 (“not at all”) to 3 (“nearly every day”). The scores are summed with a maximum score of 28. Increasing scores denote increasing depression severity.

The brief questionnaire has been well validated in the primary care population as a diagnostic and severity measure and has been shown to be a responsive and reliable measure of depression treatment outcomes (Lowe, Unutzer, Callahan, Perkins, & Kroenke, 2004). The PHQ-9 has also been recommended for use in the identification and management of depression in primary care by the New Zealand Guidelines Group (New Zealand Guidelines Group, 2008). The PHQ-9 was considered to be a more appropriate tool to assess depression outcomes in the primary care population than those recommended in the expert consensus statement for the standard research assessment of insomnia (Inventory of Depressive Symptomatology (Rush et al., 1996; Trivedi et al., 2004) or Beck Depression Inventory II (Beck et al., 1996; Carney, Ulmer, Edinger, Krystal, & Knauss, 2009)) (Buysse et al., 2006). It is recommended that depression and anxiety measures be used in insomnia research (Buysse et al., 2006) as untreated insomnia is recognised as a significant risk factor for the development of depression (Ford & Kamerow, 1989) and minor mood disturbances such as depression, worrying, anxiety, and irritability symptoms are frequently reported by those with insomnia (American Sleep Disorders Association, 2005; Moul et al., 2002).

The PHQ-9 was used as a self-completed questionnaire both prior to randomisation (to exclude those with significant depression) and as an outcome measure at baseline and at six months. For the purposes of excluding those with significant depression symptomatology, a cut point of  $\geq 9$  was used as an exclusion tool. A score of  $\geq 9$  has a likelihood ratio for major depression of 6.0 (95% sensitivity, 84% specificity) (Kroenke et al., 2001). Those patients scoring below this cut-off were considered to have minimal or mild symptoms of depression but unlikely to have a diagnosis of major depressive disorder (Kroenke et al., 2001). Therefore, only those with PHQ-9 scores below nine were included in the study. It was important to ensure outcomes were a reflection of the intervention on primary insomnia rather than on potentially co-existing depression. There was also some concern as to whether sleep restriction could worsen outcomes in those with major depression (A. Fernando, personal communication, April 21, 2009). Thus, using the PHQ-9 cut-off, those minor mood disturbances were included, but those more likely to have a moderate to severe major depression diagnosis were excluded.

## **Anxiety**

### ***GAD-7***

The generalised anxiety disorder 7-item scale (GAD-7) (R.L. Spitzer et al., 2006) is a brief 7-item self-report questionnaire asking about symptoms in the past two weeks and how frequently the responder was bothered by each symptom. The symptoms covered include feeling nervous, not being able to stop worrying, worrying too much, trouble relaxing, restlessness, becoming easily annoyed or irritable and feeling afraid something awful might happen (Kroenke et al., 2007). Response options ranged from “not at

all” (scoring 0) to “nearly every day” (scoring 3), with the global score ranging from 0 to 21. The scale was specifically designed to correlate to DSM-IV criteria, as well (American Psychiatric Association, 1994).

The inclusion of a measure for anxiety is a standard recommendation for insomnia treatment studies and is based upon the evidence of a strong relationship between insomnia symptoms and anxiety symptoms (Buysse et al., 2006; Ford & Kamerow, 1989; Ohayon, 2002) (American Sleep Disorders Association, 2005; Moul et al., 2002). The GAD-7 has been shown to be a valid and efficient tool for both diagnosing and assessing the severity of anxiety in the primary care setting. It is the recommended assessment tool for the assessment of anxiety in primary care in New Zealand (New Zealand Guidelines Group, 2008). As was the case with the depression questionnaire chosen, the GAD-7 was considered to be a more appropriate tool to assess anxiety outcomes in the primary care population than those recommended in the expert consensus statement for the standard research assessment of insomnia (State-Trait Anxiety Inventory (Spielberger, Gorsuch, & Lushene, 1970)) (Buysse et al., 2006).

The scale has been shown to have good internal and test/retest reliability as well as convergent, construct, criterion, procedural and factorial validity for the diagnosis of generalised anxiety disorder (Kroenke et al., 2007; R.L. Spitzer et al., 2006). The GAD-7 has also been shown to perform well as a screening tool for panic disorder, social anxiety disorder and post-traumatic stress disorder along with generalised anxiety disorder (Kroenke et al., 2007). Thus it represents a good measure for assessment of general anxiety conditions. A score of  $\geq 8$  has been recommended by Kroenke et al (Kroenke et al., 2007) as a reasonable cut-point for presence of clinically significant anxiety (sensitivity 0.77, 95% confidence interval, 0.70 to 0.82; specificity 0.82, 95% confidence interval, 0.80 to 0.85; positive likelihood ratio 4.4, 95% confidence interval, 3.7 to 5.2). As anxiety disorders are known to impact on sleep patterns, it was important in this trial that a primary anxiety disorder was not present (and potentially causing a secondary insomnia).

### **3.11.3 Physiological measures**

Blood pressure (BP) and resting heart rate (HR) were recorded at baseline, at the week three assessment and at the six month outcomes assessment. This monitoring was undertaken in order to ensure subjects were fit for participation with a systolic BP between 100 and 159 mmHg, diastolic BP <100 mmHg, and HR between 61 and 99 beats per minute). The BP and HR were also used to objectively measure the potential harms of the sleep restriction regimen (via monitoring for a significant change from baseline values), particularly in the initial two weeks where a mild state of sleep deprivation was anticipated. The rationale for this requirement was that changes in BP and HR were considered to be markers of potential

physiological stress associated with the intervention. Increased heart rate has been recognised as a marker of sympathetic nervous system activation (Grassi et al., 1998) and several large epidemiological studies have shown that mortality from both cardiovascular and non-cardiovascular causes generally increases with increasing heart rate (Dyer et al., 1980; Gillum, Makuc, & Feldman, 1991; Kannel, Kannel, Paffenbarger, & Cupples, 1987).

Blood pressure and resting heart rate were measured using the electronic Omron HEM-907™ (Omron Healthcare, Inc.) sphygmomanometer for blood pressure measurement by the author or a medically trained research assistant. This machine recorded blood pressure oscillometrically (“when the oscillations of pressure in a sphygmomanometer cuff are recorded during gradual deflation, the point of maximal oscillation corresponds to the mean intra-arterial pressure” (Pickering et al., 2005)). The machine used an electrostatic capacity semi-conductor pressure sensor and had a digital display showing both the blood pressure and heart rate (El Assaad, Topouchian, Darne, & Asmar, 2002). The Omron HEM-907™ has been validated as accurate and reliable for use in the clinical setting by international validation protocols (El Assaad et al., 2002; White & Anwar, 2001).

Blood pressure measurement was undertaken using the protocol recommended by the American Heart Association (Pickering et al., 2005). Using this protocol three recordings were taken with a five minute interval between each measurement and the average of the last two recordings was used as the final value (Table 3-8). A protocol was written by the author for blood pressure recording (see Appendix Z). Significant aberration of blood pressure and heart rate from the accepted normal range prompted the requirement of a medical review by the patient’s general practitioner (Table 3-8).

#### **3.11.4 Adverse events**

Motor vehicle accidents, physical injuries (requiring medical attention/not requiring medical attention), worsening angina, heart attack, strokes/transient ischaemic attacks (TIAs), hospital admissions and situations of potentially dangerous sleepiness (for example, whilst driving) were recorded at baseline, week three follow up and at six months. Significant changes in blood pressure and resting heart rate were also monitored.

*Table 3-8: Procedure for Blood Pressure and Heart Rate Recording in the ReFRaSH Trial*

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**Procedure description (Pickering et al., 2005)**

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- 1) Patient asked to remove clothing that covers the location of cuff placement
- 2) Arm circumference measured and appropriate cuff size selected
- 3) Patient should be comfortably seated, legs uncrossed, back and arm supported such that the middle of the cuff on the upper arm is at the level of the right atrium (mid-point of the sternum)
- 4) Patient is instructed to relax and rest for 5 minutes prior to the first measurement. Magazines are provided for relaxation
- 5) No talking during measurement
- 6) Three recordings taken with five minute interval between each measurement
- 7) The average of the last two recordings is used as the final value for both blood pressure and resting heart rate

### **3.12 Harms and safety monitoring**

Several measures were incorporated into the study design to assess safety. Potential harms of the trial were listed on the participant information sheet so that participants were fully informed prior to involvement in the trial (Appendix I). Those with high risk occupations were excluded prior to recruitment (for example, bus drivers or surgeons). In the second mail out questionnaire (Q2) patients were advised to see their general practitioner if they answered positively to the question about thoughts of suicide or self-harm (Appendix H). The questionnaire also stated that their general practitioner would be automatically notified by the research team if these thoughts were indicated. A protocol (developed by the author) was in place for medical attention to be sought if the pulse, blood pressure, or medical condition (positive answers to questions about chest discomfort, light headedness, shortness of breath) were outside set parameters



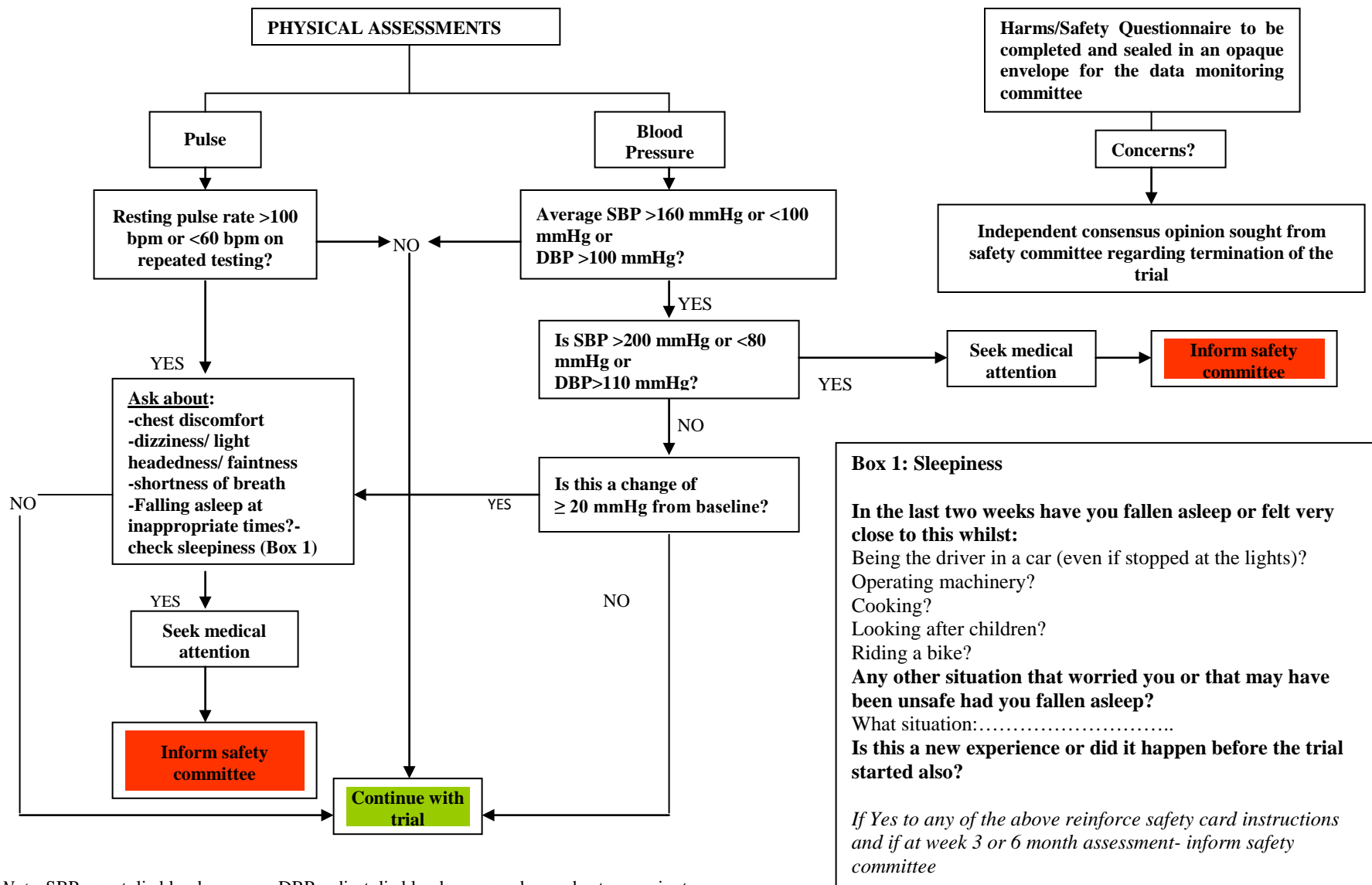
(Figure 3-4). Participants were also given a safety sheet with researcher contact details and safety advice regarding drowsiness (Appendices Q and R).

### **3.12.1 Safety monitoring committee**

Data on adverse events were monitored by the data monitoring biostatistician to assess for any signs that the intervention may be harmful. Each time the harms assessment occurred (baseline, week three, and six months), the blood pressure and heart rate measurements were recorded on the questionnaire before the participant filled in their questionnaire responses. After completing the harms assessment questionnaire, the participant sealed their questionnaire in a coded, windowless opaque envelope, which was then delivered to the research administrator who entered the data onto a spread-sheet that was forwarded to the data monitoring biostatistician. The biostatistician was blinded to the specific treatment allocations and was aware only of a generic group designation (“X” or “Y”). The biostatistician periodically reviewed the data. If a concerning trend was indicated, three steps were initiated according to the safety monitoring protocol: the research team were advised a safety committee meeting was to take place, the research administrator responsible for receiving and inputting the harms data was contacted to break the code for the committee, and a meeting of the biostatistician and an independent advisor (the safety monitoring committee) was held. If the outcome of this meeting was that a potential harm from the intervention was identified then the safety committee would meet with the research team to discuss stopping the trial. If no harm was considered to be present, the trial would continue with the research administrator giving a new designation “A” or “B” (instead of the previous X or Y) to the sleep restriction and control groups so that the biostatistician was again unaware of which group was intervention and which group was control.

### **3.13 Other Information Collected**

The first page of the comprehensive questionnaire sent to potential participants collected name, date of birth, age, ethnicity and employment status details (Appendix H). The ethnicity status was established by asking the respondent to choose as many ethnic groups as they identified with. This question was based on the ethnicity question asked in the 2006 New Zealand census. Occupation status was established by asking the respondent to choose from a list of responses (employed fulltime, employed part time, student, retired, homemaker, unemployed, sickness beneficiary).



Note. SBP = systolic blood pressure; DBP = diastolic blood pressure; bpm = beats per minute

Figure 3-4: Flowchart of harms assessment and response for the ReFRESH trial

### **3.14 Patient and General Practitioner Feedback**

The comprehensive questionnaire sent out to those who met the general criteria for insomnia had a section on the first page that could be completed with the name of the respondent's general practitioner if the respondent wished to have a copy of the questionnaire sent to their GP for inclusion into their medical records. All participants who indicated they would like to have a copy of the final results of the trial were sent a copy of the summary results once the trial was completed. A copy of the trial summary results was also sent to the doctors at each of the fourteen participating "recruitment practices".

### **3.15 Data Management**

#### **3.15.1 Data collection**

Data collection was undertaken from March 2009 until November 2012. Data entry, double-data entry, data cleaning, and data analysis continued until March 2013. The training of research assistants was performed by the author. Protocols for initial meeting, baseline appointment, week three follow up, and six month outcomes assessment were developed by the author and written prior to the commencement of data collection (Appendix AA). Protocols were also developed by the author for recruitment procedure, processing of postal responses, blood pressure measurement, sleep diary analysis, and actigraphy analysis (Appendices X-Z, AB, AC). Funding was available for a research assistant (MD, a general practitioner) for a six month period during 2010. The research assistant was trained by the author and assisted with the recruitment procedures, processing of response, and performing the six month follow up assessments. Three other casual research assistants with medical backgrounds were trained and performed six month outcome assessments over the course of the study.

Data were entered into an ACCESS program designed specifically for the ReFReSH trial by the author. All data were entered by the author. Data were then double entered by a blinded research assistant (KS). This enabled data to be checked for missing values or discrepancies. All sleep diaries and actigraphy were analysed by the author using the research protocols. To minimise the chance of error, sleep diaries were analysed twice by the author (with analyses separated in time) and the results cross checked with the actigraphy results (the overall time spent in bed should have been the same using each modality). Due to financial and time constraints a random sample of 20% of the participants (rather than all participants) had a two week period of sleep diary recordings analysed by a blinded research assistant (KS). If the error rate of the sample was greater than 0.05% overall or the sleep efficiency scores varied by greater than 0.5% overall, then the research assistant would analyse sleep diary data for all participants and any errors would be cross checked for accuracy. A further random sample of

20% of the participants had a two week sample of actigraphy recordings double analysed by a blinded assistant (AJ) familiar with the use of actigraphy software and analysis.

### **3.16 Organisation**

#### **3.16.1 Research personnel**

The author was the principal researcher who conducted the trial from the Department of General Practice, The University of Auckland and from her home in Auckland. The author was funded by a clinical research fellowship from the Health Research Council of New Zealand. For a period of six months a research assistant (MD) was employed to assist with recruitment procedures and follow up assessments. Much of the trial was conducted on a part-time basis by the author and recruitment was suspended for five months during the author's maternity leave in 2010. However, the research assistant or author were able to follow-up all participants at the correct times and according to the protocol. An additional research assistant was employed to conduct double data entry and double checking of sleep diary analyses (KS). An independent researcher conducted blinded analyses of a sample of the actigraphy data (AJ). The research assistants were funded by the Royal New Zealand College of General Practitioners Auckland Faculty Charitable Research Trust.

#### **3.16.2 Consultation**

An advisory committee was consulted for comment as the trial was being developed. This group consisted of the two supervisors: Professor Bruce Arroll and Associate Professor C. Raina Elley both from the Department of General Practice and Primary Health Care, The University of Auckland, and Dr Antonio Fernando III, psychiatrist, insomnia specialist and senior lecturer from the Department of Psychological Medicine, the University of Auckland. Dr Guy Warman and Anisoara Jardim from the Department of Anaesthesiology, The University of Auckland advised on the use of actigraphy and performed double actigraphy analyses (AJ). Alistair Stewart, senior biostatistician from the Department of Epidemiology and Biostatistics, the University of Auckland assisted with the development of randomisation procedures and the development of safety monitoring procedures for the trial and also acted as the data monitoring biostatistician. Dr Arier Chi Lun Lee from the Department of Epidemiology and Biostatistics, The University of Auckland assisted with analyses of results.

#### **3.16.3 Financial support**

Financial support for the trial was provided by the Health Research Council of New Zealand, the Royal New Zealand College of General Practitioners Auckland Faculty Charitable Research Trust, the Royal New Zealand College of General Practitioners Research and Education Charitable Fund, the School of

Medicine Foundation, the University of Auckland Department of General Practice and Primary Health Care Research Fund, and the Kate Edger Educational Charitable Trust.

### **3.17 Trial Registration and Ethical Approval**

The trial was prospectively registered with the Australian New Zealand Clinical Trial Registry ([www.anzctr.org.au](http://www.anzctr.org.au)) on 23/2/09. Trial registration number ACTRN12609000127202. Ethics approval was obtained from the Northern X Regional Ethics Committee on 24/4/08 reference number NTX/08/02/003.

## **Chapter 4 Results**

### **4.1 Introduction**

This section presents the results of the randomised controlled trial investigating the effectiveness of simplified sleep restriction for the treatment of primary insomnia in the primary care setting. The results were analysed to determine the effectiveness of the intervention with respect to the effect on the primary outcome of sleep quality and the secondary outcomes of sleepiness, fatigue, and sleep parameters. Adverse effects, including the effect on depression and anxiety were also assessed.

### **4.2 Study Participants**

Recruitment commenced March 2009 and was completed May 2012 due to a five month break in recruitment during the author's maternity leave. Follow up was completed November 2012. Seventeen general practices were identified randomly from the list of practices located in the Auckland District Health Board (ADHB) catchment area (Appendix F). Of these, fourteen general practices agreed to participate in recruiting participants for the trial (82.4%). Three general practices declined to participate. The reasons for declining to participate were the doctors being too busy to participate for two of the practices and current staff turnover making participation too difficult in the third. In total, 47 of 48 (97.9%) general practitioners working at the fourteen participating general practices agreed to participate.

In addition, 63 direct enquiries (emails and telephone calls) were received from people interested in participating in addition to those from the recruitment practices. This occurred due to a secondary recruitment procedure, which was employed to enhance the slow recruitment rate. This involved faxing information and investigator contact details to all general practices in the ADHB and Waitemata District Health Board catchment areas (Appendix AD). Practices could also elect to have a waiting room poster and/or flyers regarding the study for their practices (Appendix AE). Figure 4-1 shows the number of participants originating from each general practice.

Figure 4-2 shows the practice recruitment rate. In total, 28,978 introductory letters (Q1) were mailed out and 2,740 responses (9.5%) were received. There were 327 letters "returned to sender" due to incorrect addresses (1.1%). Of the responses received 1331 (48.6%) met the screening criteria for possible insomnia. The comprehensive questionnaire (Q2) was sent to 1,302 people (29 did not provide contact details). Of

these, 718 replies were received (55.1%). Six hundred and nine people were excluded due to having a sleep disorder other than primary insomnia, or by having a Pittsburgh Sleep Quality Index (PSQI) score less than or equal to five indicating they were “good sleepers” (Buysse et al., 1989). One hundred and nine people met the inclusion criteria by having a diagnosis of primary insomnia and having a PSQI score greater than five. Fourteen people were eligible to participate but were excluded prior to randomisation. Table 4-1 shows the reasons for exclusion.

*Table 4-1: Reasons for Exclusion Prior to Randomisation of Initially Eligible Patients in the ReFReSH Trial*

| <b>Reason for exclusion</b>                            | <b>Detail (n)</b>   |
|--|---|
| ▪ Failed physical exam                                 | Body Mass Index > 35 and Malampatti Class IV (1)<br>Heart murmur discovered which subsequently required a valve replacement (1) |
| ▪ Unable to contact                                    | (2)   |
| ▪ Change in depression medication planned              | Planning to wean fluoxetine (1)   |
| ▪ Stressful life period                                | Family crisis developed since initial contact (2)<br>Going through excessive life stress (2)                                    |
| ▪ Excessive sleepiness                                 | (3)   |
| ▪ Not meeting insomnia quantitative inclusion criteria | (2)   |

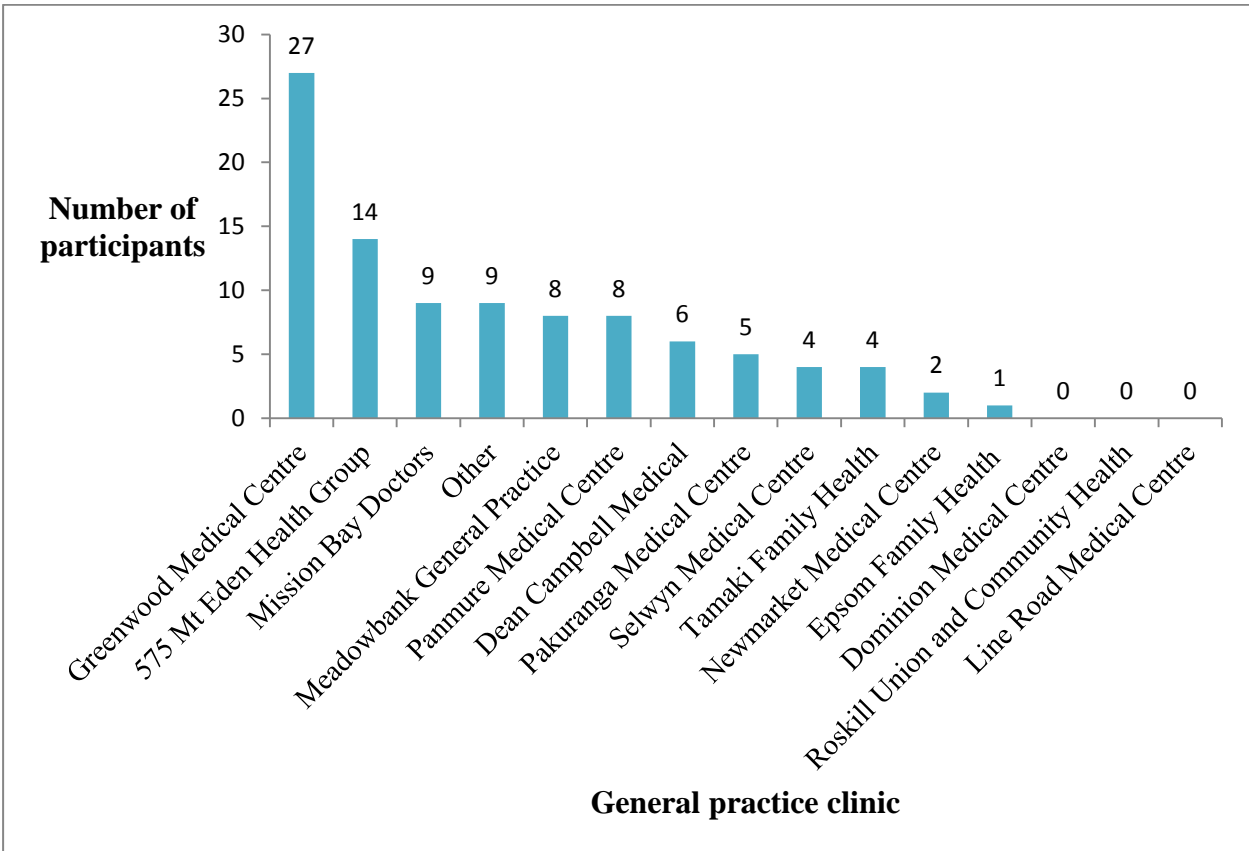


Figure 4-1: Number of participants recruited from each general practice for the ReFRaSH trial.

“Other” refers to participants recruited from direct enquiry (email or telephone) or where the general practice was not directly involved in recruitment. In this group, two participants came from the same general practitioner and the others were all from different general practitioners.

Figure 4-3 shows participant flow from enrolment through to analysis of results. Ninety seven people with primary insomnia were recruited to participate in the trial. Forty six participants were randomly allocated to the simplified sleep restriction (intervention) group and fifty one participants were randomly allocated to the control group. This fulfilled the requirement for forty five participants per group based on sample size calculations. All participants received their allocated intervention.



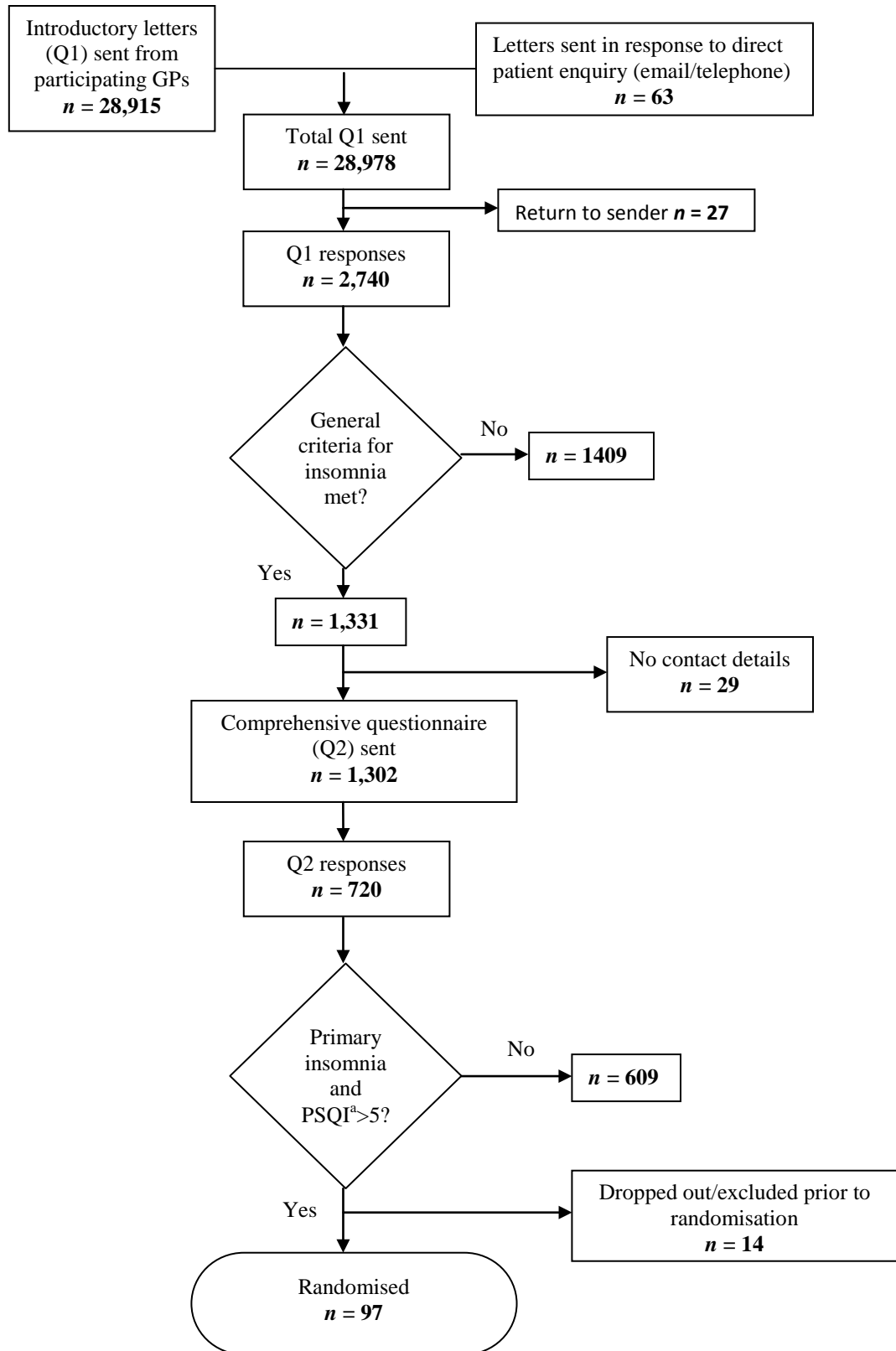


Figure 4-2: Recruitment of participants for the ReFReSH trial from primary care through to randomisation.

<sup>a</sup>Pittsburgh Sleep Quality Index (PSQI) >5 indicates a “poor sleeper” (Buysse et al., 1989)

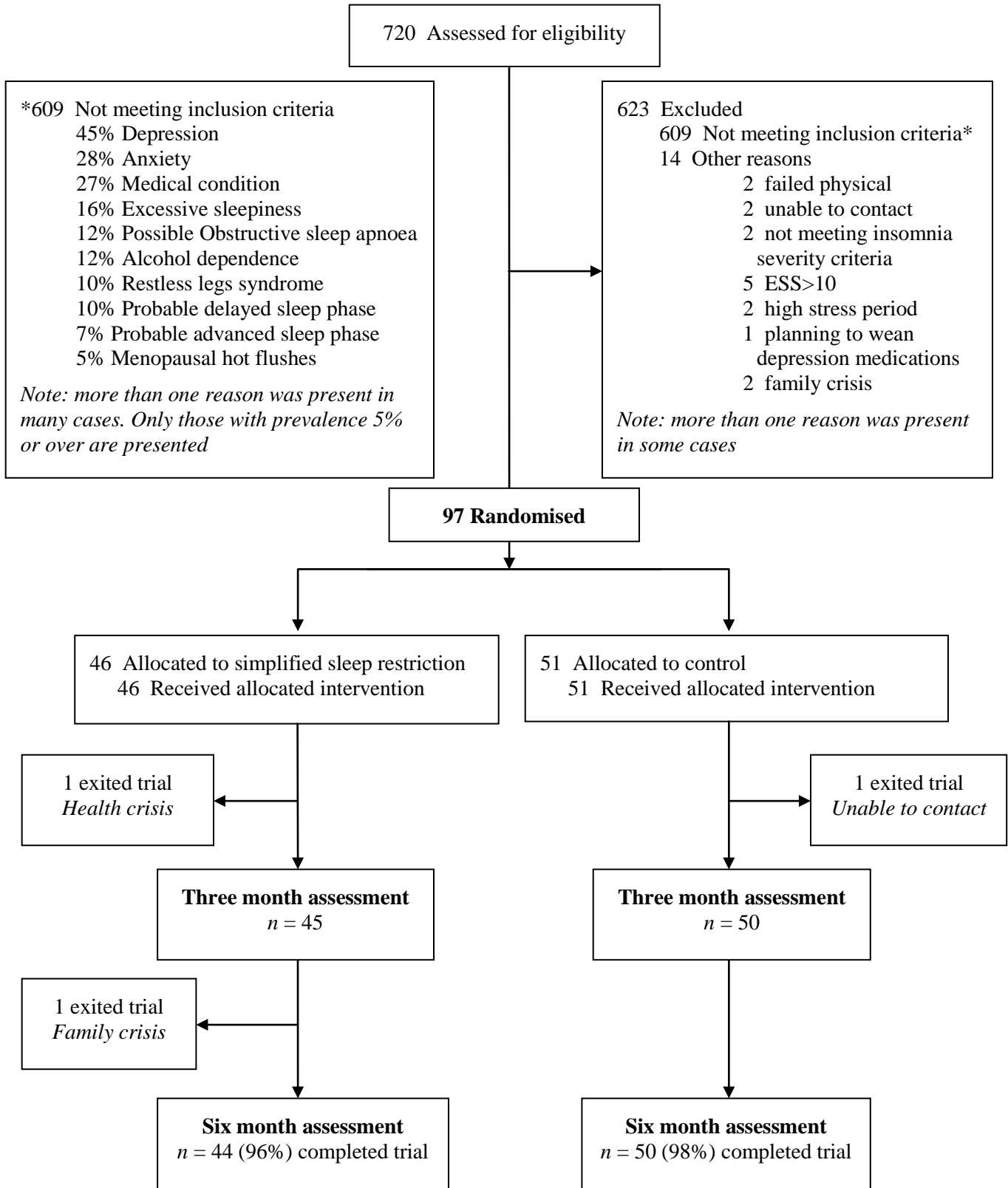


Figure 4-3: CONSORT diagram showing flow of study participants through the ReFRaSH randomised controlled trial of sleep restriction for primary insomnia

In total, forty-four participants (96%) in the simplified sleep restriction group completed the study protocol and fifty participants (98%) in the control group completed the study protocol. Two participants in the simplified sleep restriction group were lost to follow up. In the control group, one participant was lost to follow up before the three month assessment (Figure 4-3). Although the trial aimed to enroll 100 participants and only enrolled 97 (due to financial constraints), the attrition rate was considerably lower than was allowed for in the sample size calculations where 10% attrition rate had been assumed. Therefore, the final sample size was still greater than the estimated 90 required for adequate statistical power.

After randomisation, two participants (one in each group) were found to not meet inclusion criteria as their PSQI scores were less than or equal to five (calculation error). These participants were included in the results analysis as per the intention-to-treat protocol. Table 4-2 shows the missing data.

*Table 4-2: Missing Data for Participants of the ReFReSH Trial*

| <b>Missing data</b>       | <b>Simplified sleep restriction</b> | <b>Control</b>   |
|---------------------------|-------------------------------------|------------------|
| Three month questionnaire | 1 <sup>a</sup>                      | 2 <sup>bc</sup>  |
| Six month                 |                                     |                  |
| Questionnaire             | 3 <sup>ade</sup>                    | 1 <sup>c</sup>   |
| Sleep diary               | 3 <sup>aef</sup>                    | 2 <sup>cg</sup>  |
| Actigraphy                | 4 <sup>aefh</sup>                   | 2 <sup>cg</sup>  |
| Physiological measures    | 3 <sup>aef</sup>                    | 3 <sup>cgi</sup> |

*Note.* <sup>a</sup> drop out a 2 weeks due to health crisis. <sup>b</sup> questionnaire not returned. <sup>c</sup> unable to contact. <sup>d</sup> moved overseas. <sup>e</sup> family crisis. <sup>f</sup> “too busy”. <sup>g</sup> “sick of thinking about sleep”. <sup>h</sup> Actiwatch malfunction. <sup>i</sup> unable to attend the appointment.

As well as those who did not complete follow up assessments as mentioned above, there were six participants who had follow up measures only partially completed at one time point. In the simplified sleep restriction group one participant was missing six month actigraphy data only (Actiwatch malfunction), one participant was missing six month sleep diary, actigraphy data, and physiological measures (“too busy”),

and one participant was missing the six month questionnaire only (moved overseas before collection). In the control group, one participant was missing the three month questionnaire (but had completed six month follow up), one participant was missing sleep diary, actigraphy data, and physiological measures for the six month follow up (“sick of thinking about sleep”), and one participant was missing only the physiological measures for the six month follow up (unable to attend appointment).

Due to resource constraints, blinded outcomes assessments were performed in only 41% (37/91) of those who completed full outcomes assessment (18 in the simplified sleep restriction groups and 19 in the control group). Assessment consisted of self-report questionnaire, blood pressure, heart rate and weight measurement. The remainder of the participants had their outcomes assessed by the author whereby the participant signed to verify the accuracy of the digitally-recorded blood pressure, heart rate and weight recordings in order to minimise the risk of assessment bias.

## **4.3 Baseline Data**

### **4.3.1 Participant demographic characteristics**

Baseline participant demographic and sleep related characteristics are presented in Table 4-3. The simplified sleep restriction and control groups had similar baseline and demographic characteristics. However, there was a slightly higher percentage of females in the simplified sleep restriction group compared to the control group (85% vs 71% respectively), and the simplified sleep restriction group consumed an average of one unit of caffeine less, per day. Even so, participant sleep measures and clinical characteristics were well balanced, suggesting adequate randomisation (Table 4-3). Overall, 77% of participants were female ( $n = 75$ ) and the mean age of all participants was 53.5 years (SD 13.1).

The ethnicity of the study participants was 96% New Zealand European with 2% Maori and 3% Asian participants. This is compared to the proportions of 65% New Zealand European, 14% Maori and 9% Asian nationally (Statistics New Zealand, 2013). Sixty one percent of participants had previously consulted their general practitioner (GP) regarding their insomnia. For those who did not consult their GP, the most frequently cited reason was that their difficulty sleeping was “not important enough”. Figure 4-4 shows the reasons why participants did not seek help from their GP.

Table 4-3: Baseline Demographic and Sleep-Related Characteristics for the Participants in the ReFRReSH Trial

| Characteristic                            | Simplified sleep restriction<br><i>n</i> = 46 | Control<br><i>n</i> = 51 |
|---|---|--------------------------|
| Age, years                                | 55.4 (12.7)                                   | 51.8 (13.4)              |
| Female                                    | 39 (85)                                       | 36 (71)                  |
| Ethnicity <sup>a</sup>                    |   |                          |
| NZ European                               | 45 (98)                                       | 48 (94)                  |
| Maori                                     | 1 (2)   | 1 (2)                    |
| Asian                                     | 0   | 3 (6)                    |
| Other                                     | 2 (4)   | 1 (2)                    |
| Occupation status <sup>b</sup>            |   |                          |
| Full time work                            | 18 (39)                                       | 21 (41)                  |
| Part time work                            | 13 (28)                                       | 19 (37)                  |
| Retired                                   | 10 (22)                                       | 6 (12)                   |
| Homemaker                                 | 1 (2)   | 3 (6)                    |
| Student                                   | 1 (2)   | 2 (4)                    |
| Unemployed                                | 1 (2)   | 0                        |
| Duration of insomnia, years               | 15 (14)                                       | 14 (13)                  |
| Sleeping medication use <sup>c</sup>      |   |                          |
| None                                      | 28 (61)                                       | 31 (61)                  |
| < 1x per week                             | 5 (11)  | 3 (6)                    |
| 1-2x per week                             | 5(11)   | 5 (10)                   |
| ≥ 3x per week                             | 8 (17)  | 12 (24)                  |
| Caffeine, units per day                   | 2.7 (1.9)                                     | 3.7 (2.0)                |
| Alcohol, units per week                   | 4.0 (4.0)                                     | 4.9 (7.7)                |
| Prescribed medications,<br>number per day | 1.5 (2.4)                                     | 1.2 (1.7)                |

*Note.* Unless otherwise indicated, data are reported as number (percentage) or mean (SD). <sup>a</sup>Some participants identified as more than one ethnic group. <sup>b</sup>Data were missing for two participants in the sleep restriction group therefore the percentages do not add up to one hundred. <sup>c</sup>Use of sleeping medication in the month preceding completion of the Q2 questionnaire. The categories correspond to those used in the Pittsburgh Sleep Quality Index sleep medication component (Buysse et al., 1989).

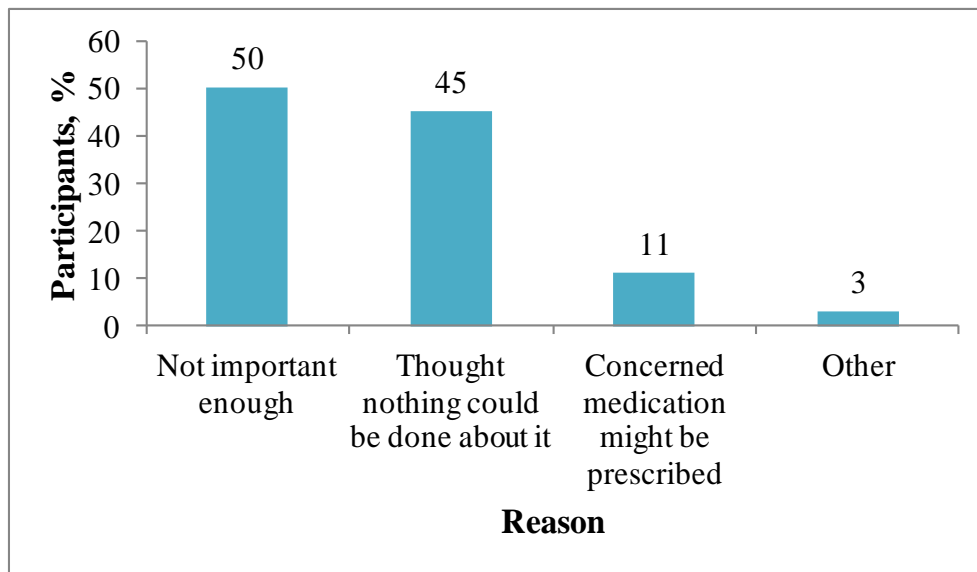


Figure 4-4: Reasons for not seeking help from the general practitioner for insomnia in participants in the ReFRReSH trial

### 4.3.2 Participant sleep and clinical characteristics

The baseline sleep measures and clinical characteristics for participants in the trial are shown in Table 4-4. Subjective sleep quality as measured by the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989) and the Insomnia Severity Index (ISI) (Bastien et al., 2001) were very similar between the two groups. The mean scores for the simplified sleep restriction group were 10.4 ( $SD = 3.1$ ) and 14.8 (3.9), for the PSQI and ISI, respectively, and the mean scores for the control group were 10.3 (3.0) and 14.5 (3.4), respectively. The mean insomnia severity of both the sleep restriction group and the control groups fell between the “subthreshold insomnia” (scores 8-14) and the “moderate clinical insomnia” (scores 14-20) subcategories of the ISI (Bastien et al., 2001). Figure 4-5 shows the percentage of participants in each group according to ISI subcategory. One participant in the control group had “no insomnia” as measured by the ISI, as this index was not used as an inclusion criterion. Both the simplified sleep restriction group and the control group had similar baseline levels of fatigue as measured by the Flinders Fatigue Scale (FFS) (Grasidar et al., 2007). Clinical cut off scores have not been defined for the FFS; however, as summary scores can range from 0-31, the baseline scores for the participants fell in the low-to-moderate range. At baseline, participants slept for an average of six hours each night with a sleep efficiency of 73-74%. Physiological measures were similar between groups apart from the mean heart rate, which was slightly higher in the control group than in the simplified sleep restriction group (73 vs 69 beats per minute).

Table 4-4: Baseline Sleep Measures and Clinical Characteristics for the Participants in the ReFR<sub>e</sub>SH Trial

| Characteristic                                  | Simplified sleep restriction<br>mean (SD) <i>n</i> = 46 | Control<br>mean (SD) <i>n</i> = 51 |
|---|---|------------------------------------|
| <b>Primary outcomes</b>                         |   |                                    |
| Pittsburgh Sleep Quality Index <sup>a</sup>     | 10.4 (3.1)  | 10.3 (3.0)                         |
| Insomnia Severity Index <sup>b</sup>            | 14.8 (3.9)  | 14.5 (3.4)                         |
| Sleep efficiency [sleep diary] <sup>c</sup> , % | 73.3 (11.8)   | 74.2 (11.1)                        |
| Sleep efficiency [actigraphy], %                | 82.7 (4.7)  | 82.4 (4.7)                         |
| <b>Secondary outcomes - sleep</b>               |   |                                    |
| Epworth Sleepiness Scale <sup>d</sup>           | 5.2 (3.7)   | 6.5 (3.3)                          |
| Flinders Fatigue Scale <sup>e</sup>             | 12.7 (6.8)  | 12.5 (5.1)                         |
| Sleep onset latency, min                        |   |                                    |
| Sleep diary                                     | 31.5 (23.0)   | 29.6 (22.5)                        |
| Actigraphy                                      | 16.1 (14.5)   | 14.7 (12.4)                        |
| Wake after sleep onset, min                     |   |                                    |
| Sleep diary                                     | 44.8 (28.9)   | 47.8 (30.1)                        |
| Actigraphy                                      | 47.6 (13.9)   | 51.8 (19.5)                        |
| Total sleep time, min                           |   |                                    |
| Sleep diary                                     | 369.6 (65.3)  | 376.9 (61.1)                       |
| Actigraphy                                      | 415.7 (34.2)  | 418.4 (39.4)                       |
| <b>Secondary outcomes – mental health</b>       |   |                                    |
| PHQ-9 depression score <sup>f</sup>             | 5.0 (2.8)   | 5.3 (2.8)                          |
| GAD-7 anxiety score <sup>g</sup>                | 3.3 (3.1)   | 3.4 (2.5)                          |
| <b>Physiological measures</b>                   |   |                                    |
| Systolic blood pressure, mmHg                   | 122.2 (14.0)  | 123.9 (13.2) <sup>h</sup>          |
| Diastolic blood pressure, mmHg                  | 75.5 (10.4)   | 75.6 (9.0) <sup>h</sup>            |
| Heart rate, beats per minute                    | 68.9 (9.8)  | 73.3 (10.9)                        |
| Body mass index, kg/m <sup>2</sup>              | 25.8 (3.9)  | 25.2 (4.3)                         |

Note. <sup>a</sup> (Buysse et al., 1989). <sup>b</sup> (Bastien et al., 2001). <sup>c</sup> Using data averaged from sleep diary recordings for a two week period. Sleep efficiency is calculated as total sleep time (TST)/time spent in bed (TIB) x 100%. <sup>d</sup> (Johns, 1991). <sup>e</sup> (Grasidar et al., 2007). <sup>f</sup> Patient Health Questionnaire-9 (Kroenke et al., 2001). <sup>g</sup> Generalised Anxiety Disorders-7 (R.L. Spitzer et al., 2006). <sup>h</sup> *n* = 50 due to equipment malfunction.

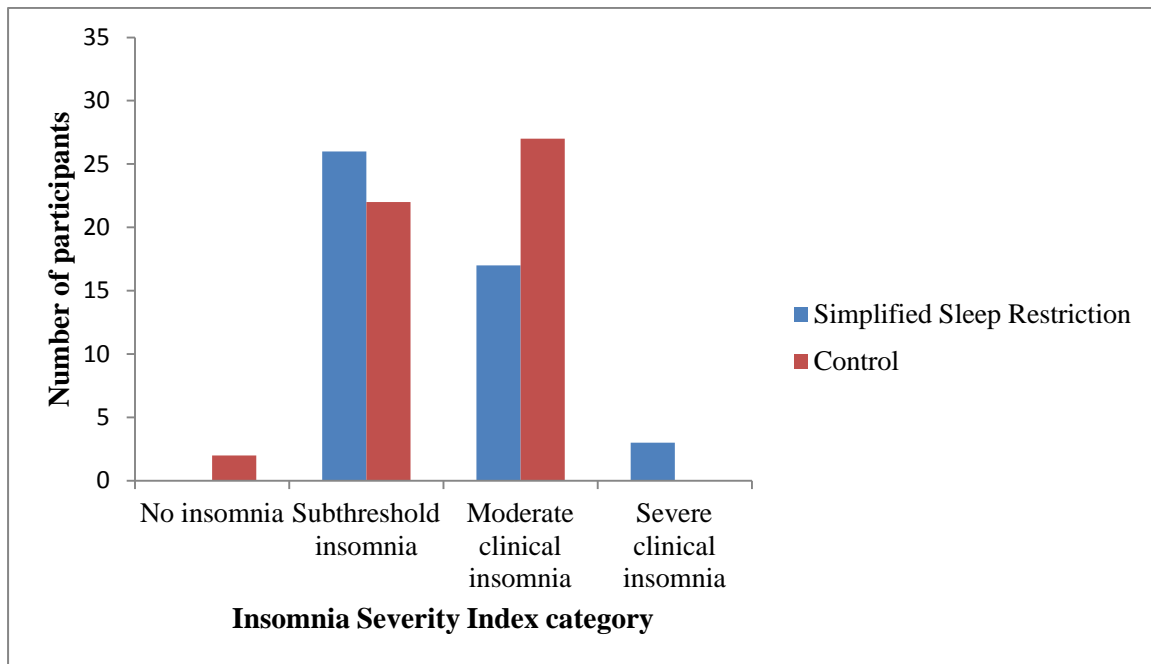


Figure 4-5: Baseline Insomnia Severity Index category for participants in each group of the ReFRaSH trial.

Insomnia Severity Index (Bastien et al., 2001). Simplified sleep restriction group n = 46, control group n = 51.

### Previous exposure to insomnia treatments

Figure 4-6 shows the insomnia treatments known by participants in the trial. Prescription medication was the treatment most known by the participants with 80% (87/97) aware of this treatment. Self-medication with herbal and over-the-counter treatments and relaxation strategies including meditation and yoga were the next treatment types most commonly reported by participants (53% and 49%, respectively). Very few participants were aware of behavioural methods or specific sleep strategies for the treatment of insomnia. One participant had a basic idea of sleep restriction having just attended a company workshop from a sleep specialist.

Figure 4-7 shows the insomnia treatments previously tried by the participants in the trial. Prescription medication was the most common previously tried treatment. However, only 47% (46/97) of participants had actually used prescription sleep medications in the past, despite most being aware of this treatment option. Self-medication with herbal and over-the-counter treatments was the next most common previously tried treatment. Only 4% (4/97) had previously tried behavioural techniques despite 61% having sought help from their GP for insomnia. The one participant who was aware of sleep restriction as a treatment had



not tried this technique and 16% (16/97) of participants had not tried any treatments for insomnia. These results suggest that there is a wide variety of options available to those who suffer from insomnia but little use of evidence-based non-pharmacological treatment options.

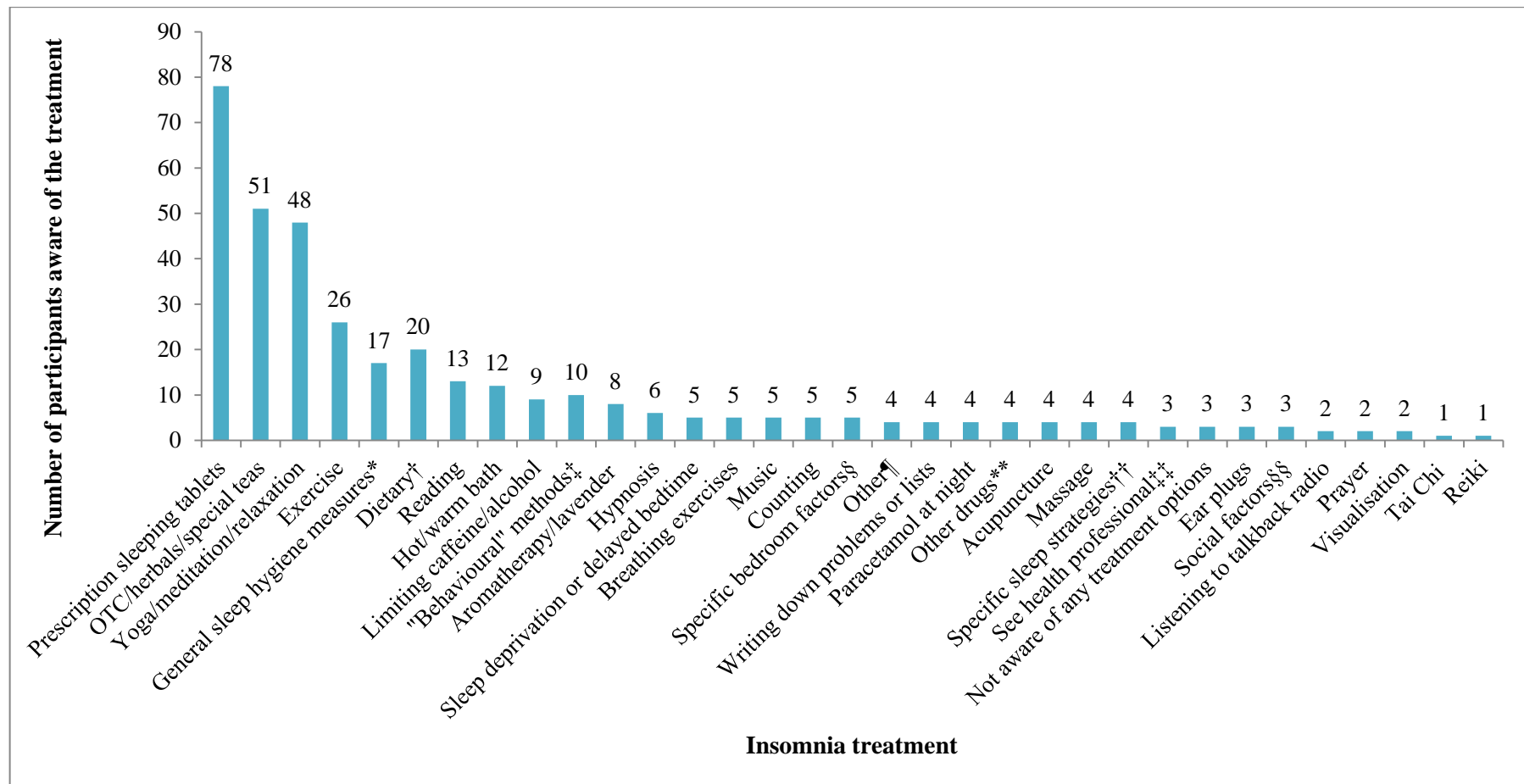


Figure 4-6: Insomnia treatments **known** by participants in the ReFReSH trial at baseline.

Abbreviations: OTC – over the counter medications. \*General sleep hygiene measures: included “sleep hygiene” and single components of sleep hygiene. †Dietary measures included warm milk, Milo, banana, lecithin. ‡“Behavioural” methods: listed as “behavioural” plus strategies such as getting out of bed if unable to sleep, going to bed early and dim light 1h before bedtime. §Specific bedroom factors: moving to another bed, sleep pillows, blackout curtains, comfortable bed. ¶Other: watching TV, singing repetitively, cleaning rooms and one participant was also aware of painting the bedroom pale blue, wearing a face mask with 3oz pressure over each eye and taping their mouth closed with Micropore tape. \*\*Other drugs: antihistamines, antidepressants, alcohol and marijuana. ††Specific sleep strategies included: “special watch”, “special classes”, and “Sleep Therapy” described as “medically-induced sleep for three days”. ‡‡Health professional included: seeing General Practitioner, sleep clinic, and cognitive behavioural therapy. §§Social factors included: good relationships, being romantic, no financial stress. Treatments were categorised during analysis of questionnaire responses.

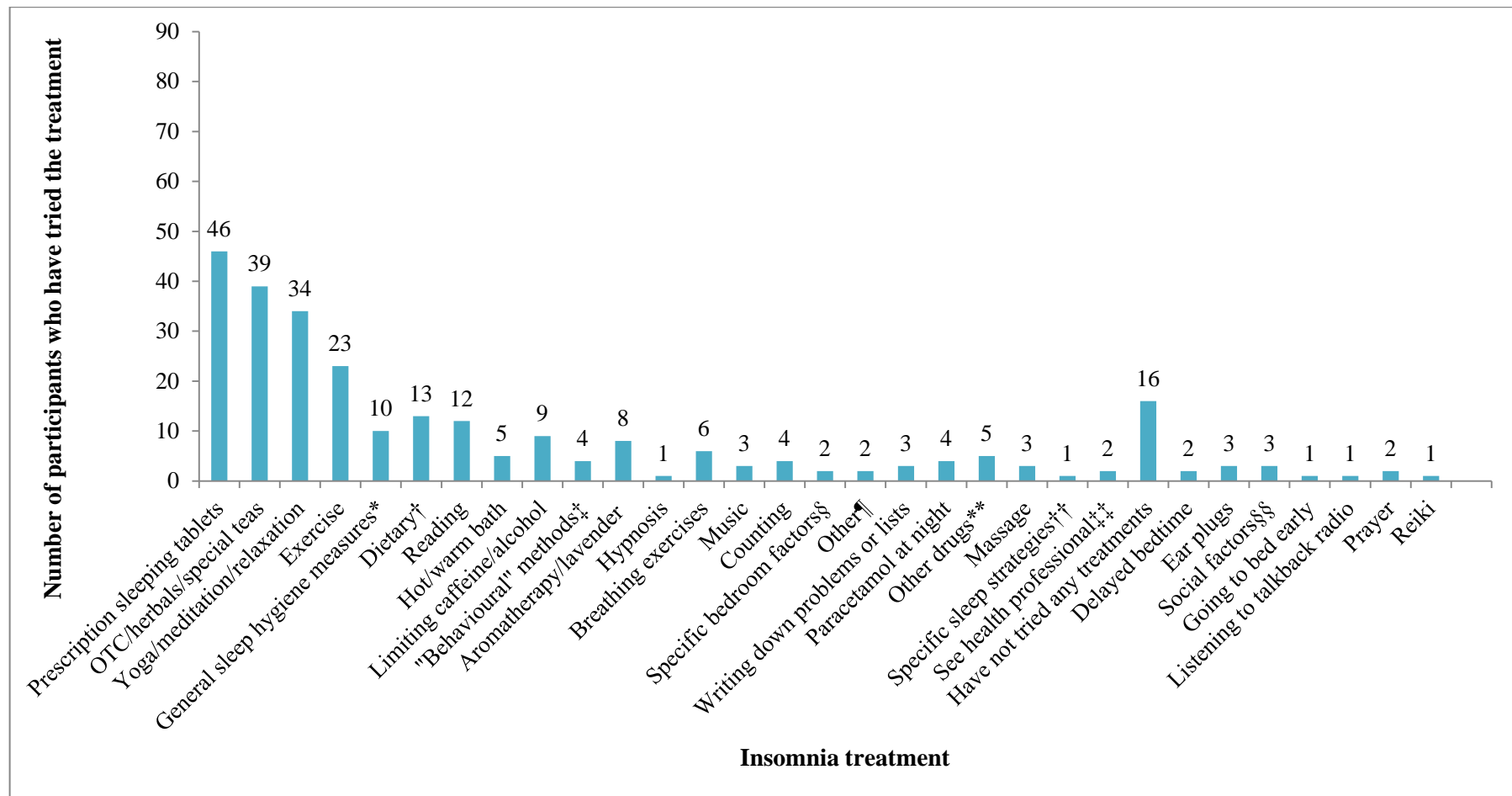


Figure 4-7: Insomnia treatments *previously tried* by participants in the ReFRESH trial at baseline.

Abbreviations: OTC – over the counter medications. \*General sleep hygiene measures: included “sleep hygiene” and single components of sleep hygiene. †Dietary measures included warm milk, Milo, banana, lecithin. ‡“Behavioural” methods: listed as “behavioural” plus strategies such as getting out of bed if unable to sleep and going to bed early. §Specific bedroom factors: moving to another bed and comfortable bed. ¶Other: singing repetitively and one participant had also tried painting the bedroom pale blue, a face mask with 3oz pressure over each eye and taping their mouth closed with Micropore tape. \*\*Other drugs: antihistamines, antidepressants, alcohol and marijuana. ††Specific sleep strategies – Continuous positive airways pressure (CPAP). ‡‡Health professional included: seeing General Practitioner and cognitive behavioural therapy. §§Social factors included: good relationships, being romantic, no financial stress. Treatments were categorised during analysis of questionnaire responses.

## 4.4 Numbers Analysed

Follow-up data were incomplete in nine participants due to withdrawing from the study after randomisation ( $n = 3$ ), participant refusal ( $n = 3$ ), and data collection errors ( $n = 3$ ). The rates of missing data were calculated with each participant having five possible data collections: questionnaire at three months; and questionnaire, sleep diary, actigraphy, and physiological measurements at six months. The overall rates of missing data were 0.05% (24/485 data items). As the overall rate of missing data was low and the reasons for missing data appeared relatively balanced across the groups (10 data items missing from control group and 14 data items missing from the simplified sleep restriction group) no imputations of data were made. As per the intention-to-treat protocol, participants were analysed according to their originally assigned groups.

## 4.5 Outcomes and Estimation

### 4.5.1 Summary results

The mean duration of advice given at the initial visit was 20 minutes for the simplified sleep restriction group and 11 minutes for the control group. The mean duration of advice given at the second visit was 14 minutes and 11 minutes, respectively.

Table 4-5 shows the summary results for the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989) and Insomnia Severity Index (ISI) (Bastien et al., 2001). Both outcomes showed a statistically significant improvement with the simplified sleep restriction treatment compared with the control treatment when measured at six months ( $p < 0.001$  and  $p = 0.001$ , respectively). This suggested that the simplified sleep restriction treatment led to subjective improvements in sleep quality. Further results for PSQI and ISI are presented individually in Section 4.6.2.

Tables 4-6 to 4-9 show the summary results for the variables that had data recorded at baseline and six months which were analysed using a general linear model. This included the primary outcome of sleep efficiency (%) and the secondary outcomes of sleep and mental health measures. There was a small statistically significant difference in the adjusted mean differences (from baseline to six months) between the simplified sleep restriction and control groups in fatigue (measured by the Flinders Fatigue Scale (Grasidar et al., 2007)) and sleep onset latency (measured by actigraphy but not by sleep diary) ( $p = 0.04$ ). These differences suggested a greater reduction in levels of fatigue and a shorter time to fall asleep

experienced by the simplified sleep restriction group. There was also a statistically significant improvement in sleep efficiency in the simplified sleep restriction group when measured by actigraphy ( $p = 0.006$ ). These results are discussed further in Section 4.6.3.

Table 4-5: Pittsburgh Sleep Quality Index and Insomnia Severity Index Results Assessed at Baseline, Three, and Six Months in the ReFReSH Trial of Simplified Sleep Restriction for Primary Insomnia

|   | Simplified sleep restriction                            |  |  | Control   |  |  | Difference between the groups, [95% CI], <i>p</i> value <sup>b</sup> | Effect size <sup>e</sup> |
|---|---|--|--|---|--|--|--|--------------------------|
|   | Baseline score, mean (SD) <sup>a</sup><br><i>n</i> = 46 | Three month score, mean (SD) <sup>a</sup><br><i>n</i> = 45 | Six month score, mean (SD) <sup>a</sup><br><i>n</i> = 43 | Baseline score, mean (SD) <sup>a</sup><br><i>n</i> = 51 | Three month score, mean (SD) <sup>a</sup><br><i>n</i> = 49 | Six month score, mean (SD) <sup>a</sup><br><i>n</i> = 50 |  |                          |
| <b>Primary outcomes</b>                     |   |  |  |   |  |  |  |                          |
| Pittsburgh Sleep Quality Index <sup>c</sup> | 10.43 (3.08)  | 6.24 (3.11)  | 6.49 (3.52)  | 10.29 (3.02)  | 8.71 (3.32)  | 8.10 (3.49)  | -2.14<br>[-3.15, -1.13]<br><b>&lt;0.0001</b>                         | 0.54                     |
| Insomnia Severity Index <sup>d</sup>        | 14.76 (3.85)  | 8.47 (4.45)  | 8.28 (4.41)  | 14.51 (3.36)  | 11.51 (3.94)   | 10.50 (3.72)   | -2.50<br>[-3.97, -1.03]<br><b>0.001</b>                              | 0.50                     |

Note. Statistically significant results are printed in bold. <sup>a</sup>Observed (raw) data. <sup>b</sup>Mixed model for repeated measures adjusted for age, gender and baseline insomnia severity (using ISI score). <sup>c</sup>PSQI (Buysse et al., 1989). <sup>d</sup>ISI (Bastien et al., 2001). <sup>e</sup>Unadjusted effect size = (mean observed difference sleep restriction group – mean observed difference control group)/pooled standard deviation of the mean observed differences.

Table 4-6: Sleep Efficiency Results Assessed at Baseline and Six Months in the ReFReSH Trial of Simplified Sleep Restriction for Primary Insomnia

|                                   | Simplified sleep restriction                            |  |   | Control   |  |   | Difference between the groups <sup>bd</sup> , [95% CI], <i>p</i> value | Effect size <sup>e</sup> |
|-----------------------------------|---|--|---|---|--|---|--|--------------------------|
|                                   | Baseline score, mean (SD) <sup>a</sup><br><i>n</i> = 46 | Six month score, mean (SD) <sup>a</sup><br><i>n</i> = 44 | Least square mean for change [95% CI] <sup>bc</sup> | Baseline score, mean (SD) <sup>a</sup><br><i>n</i> = 51 | Six month score, mean (SD) <sup>a</sup><br><i>n</i> = 50 | Least square mean for change [95% CI] <sup>bc</sup> |  |                          |
| <b>Primary outcomes</b>           |   |  |   |   |  |   |  |                          |
| Sleep efficiency (sleep diary), % | 73.32 (11.80)   | 80.46 (10.66) <sup>f</sup>                               | 6.72 [3.90, 9.54]                                   | 74.15 (11.05)   | 78.24 (10.52) <sup>g</sup>                               | 4.28 [-6.70, 1.86]                                  | 2.44 [-0.96, 5.84]<br>0.2  | 0.36                     |
| Sleep efficiency (actigraphy), %  | 82.68 (4.66)  | 83.74 (4.94) <sup>h</sup>                                | 1.75 [0.42, 3.09]                                   | 82.37 (4.67)  | 81.96 (5.38) <sup>g</sup>                                | -0.46 [-1.58, 0.65]                                 | 2.22 [0.65, 3.79]<br><b>0.006</b>                                      | 0.55                     |

Note. <sup>a</sup>Observed (raw) data. <sup>b</sup>Multiple linear regression adjusted for age, gender and baseline insomnia severity (using Insomnia Severity Index score (Bastien et al., 2001)). <sup>c</sup>Least square mean for change from baseline to six month score. <sup>d</sup>Least square mean difference for change from baseline to six months score between sleep restriction and control group. <sup>e</sup>Unadjusted effect size = (mean observed difference sleep restriction group – mean observed difference control group)/pooled standard deviation of the mean observed differences. <sup>f</sup>*n* = 43. <sup>g</sup>*n* = 49. <sup>h</sup>*n* = 42.

Table 4-7: Sleepiness and Fatigue Assessed at Baseline and Six Months in the ReFReSH Trial of Simplified Sleep Restriction for Primary Insomnia

|   | Simplified sleep restriction                            |  |   | Control   |  |   | Difference between the groups <sup>bd</sup> , [95% CI], <i>p</i> value | Effect size <sup>e</sup> |
|---|---|--|---|---|--|---|--|--------------------------|
|   | Baseline score, mean (SD) <sup>a</sup><br><i>n</i> = 46 | Six month score, mean (SD) <sup>a</sup><br><i>n</i> = 43 | Least square mean for change [95% CI] <sup>bc</sup> | Baseline score, mean (SD) <sup>a</sup><br><i>n</i> = 51 | Six month score, mean (SD) <sup>a</sup><br><i>n</i> = 50 | Least square mean for change [95% CI] <sup>bc</sup> |  |                          |
| Epworth Sleepiness Scale (ESS) <sup>f</sup> | 5.17 (3.70)   | 3.70 (2.93)  | -1.62<br>[-2.72, -0.53]                             | 6.45 (3.29)   | 4.86 (3.28)  | -1.55<br>[-2.50, -0.61]                             | -0.07,<br>[-1.40, 1.27]<br>0.9   | 0.01                     |
| Flinders Fatigue Scale (FFS) <sup>g</sup>   | 12.74 (6.83)  | 7.30 (5.49)  | -5.39<br>[-7.16, -3.63]                             | 12.53 (5.11)  | 9.08 (4.96)  | -3.12<br>[-4.65, -1.59]                             | -2.27,<br>[-4.42, -0.13]<br><b>0.04</b>                                | 0.33                     |

*Note.* Statistically significant results are printed in bold. <sup>a</sup>Observed (raw) data. <sup>b</sup>Multiple linear regression adjusted for age, gender and baseline insomnia severity (using Insomnia Severity Index score (Bastien et al., 2001)). <sup>c</sup>Least square mean for change from baseline to six month score. <sup>d</sup>Least square mean difference for change from baseline to six months score between sleep restriction and control group. <sup>e</sup>Unadjusted effect size = (mean observed difference sleep restriction group – mean observed difference control group)/pooled standard deviation of the mean observed differences. <sup>f</sup>ESS (Johns, 1991). <sup>g</sup>FFS (Grasidar et al., 2007).



Table 4-8: Sleep Outcomes Assessed at Baseline and Six-Months in the ReFRReSH Trial of Simplified Sleep Restriction for Primary Insomnia

|                             | Simplified sleep restriction                            |  |   | Control   |  |   | Difference between the groups <sup>bd</sup> , [95% CI], <i>p</i> value | Effect size <sup>e</sup> |
|-----------------------------|---|--|---|---|--|---|--|--------------------------|
|                             | Baseline score, mean (SD) <sup>a</sup><br><i>n</i> = 46 | Six month score, mean (SD) <sup>a</sup><br><i>n</i> = 43 | Least square mean for change [95% CI] <sup>bc</sup> | Baseline score, mean (SD) <sup>a</sup><br><i>n</i> = 51 | Six month score, mean (SD) <sup>a</sup><br><i>n</i> = 50 | Least square mean for change [95% CI] <sup>bc</sup> |  |                          |
| Sleep onset latency, min    |   |  |   |   |  |   |  |                          |
| Sleep diary                 | 31.50<br>(23.00)  | 22.77<br>(19.60)   | -6.29<br>[-12.75, 0.16]                             | 29.55<br>(22.48)  | 25.21<br>(19.38) <sup>f</sup>                            | -2.84<br>[-8.38, 2.70]                              | -3.45<br>[-11.23, 4.32]<br>0.4   | 0.25                     |
| Actigraphy                  | 16.10<br>(14.47)  | 13.37<br>(7.91) <sup>g</sup>                             | -5.08<br>[-9.90, -0.26]                             | 14.66<br>(12.42)  | 15.61<br>(12.74) <sup>f</sup>                            | 1.06<br>[-2.97, 5.08]                               | -6.13<br>[-11.82, -0.44]<br><b>0.04</b>                                | 0.43                     |
| Wake after sleep onset, min |   |  |   |   |  |   |  |                          |
| Sleep diary                 | 44.82<br>(28.92)  | 29.47<br>(31.71)   | -13.37<br>[-22.69, -4.05]                           | 47.84<br>(30.14)  | 40.02<br>(27.00) <sup>f</sup>                            | -7.61<br>[-15.60, 0.39]                             | -5.76<br>[-17.00, 5.47]<br>0.3   | 0.24                     |
| Actigraphy                  | 47.59<br>(13.88)  | 44.33<br>(15.44) <sup>g</sup>                            | -4.54<br>[-8.99, -0.08]                             | 51.81<br>(19.51)  | 51.59<br>(17.50) <sup>f</sup>                            | -1.46<br>[-5.18, 2.27]                              | -3.08<br>[-8.35, 2.18]<br>0.2  | 0.21                     |
| Total sleep time, min       |   |  |   |   |  |   |  |                          |
| Sleep diary                 | 369.59<br>(65.27)                                       | 397.30<br>(63.29)  | 23.71<br>[9.51, 37.90]                              | 376.93<br>(61.08)                                       | 398.17<br>(64.91) <sup>f</sup>                           | 18.99<br>[6.81, 31.67]                              | 4.72<br>[-12.39, 21.83]<br>0.6   | 0.21                     |
| Actigraphy                  | 415.68<br>(34.17)                                       | 407.20<br>(36.92) <sup>g</sup>                           | -7.00<br>[-15.94, 1.95]                             | 418.36<br>(39.36)                                       | 415.05<br>(38.45) <sup>f</sup>                           | -7.10<br>[-14.58, 0.38]                             | 0.10<br>[-10.47, 10.67]<br>0.99  | 0.02                     |

Note. Statistically significant results are printed in bold. <sup>a</sup>Observed (raw) data. <sup>b</sup>Multiple linear regression adjusted for age, gender and baseline insomnia severity (using Insomnia Severity Index score (Bastien et al., 2001)). <sup>c</sup>Least square mean for change from baseline to six month score. <sup>d</sup>Least square mean difference for change from baseline to six months score between sleep restriction and control group. <sup>e</sup>Unadjusted effect size = (mean observed difference sleep restriction group – mean observed difference control group)/pooled standard deviation of the mean observed differences <sup>f</sup>*n* = 49. <sup>g</sup>*n* = 42.

Table 4-9: Mental Health Outcomes Assessed at Baseline and Six Months in the ReFReSH Trial of Sleep Restriction for Primary Insomnia

|   | Simplified sleep restriction                            |  |   | Control   |  |   | Difference between the groups <sup>bd</sup> , [95% CI], <i>p</i> value | Effect size <sup>e</sup> |
|---|---|--|---|---|--|---|--|--------------------------|
|   | Baseline score, mean (SD) <sup>a</sup><br><i>n</i> = 46 | Six month score, mean (SD) <sup>a</sup><br><i>n</i> = 43 | Least square mean for change [95% CI] <sup>bc</sup> | Baseline score, mean (SD) <sup>a</sup><br><i>n</i> = 51 | Six month score, mean (SD) <sup>a</sup><br><i>n</i> = 50 | Least square mean for change [95% CI] <sup>bc</sup> |  |                          |
| <b>Secondary outcomes – mental health</b> |   |  |   |   |  |   |  |                          |
| PHQ-9 depression score <sup>f</sup>       | 4.98 (2.76)   | 2.93 (2.39)  | -2.19<br>[-3.21, -1.17]                             | 5.31 (2.80)   | 3.62 (2.69)  | -1.66<br>[-2.54, -0.78]                             | -0.53<br>[-1.77, 0.71]<br>0.4  | 0.1                      |
| GAD-7 anxiety score <sup>g</sup>          | 3.33 (3.06)   | 1.47 (1.88)  | -1.76<br>[-2.59, -0.92]                             | 3.41 (2.45)   | 2.56 (2.35)  | -0.84<br>[-1.56, -0.12]                             | -0.92<br>[-1.93, 0.10]<br>0.08   | 0.33                     |

Note. Statistically significant results are printed in bold. <sup>a</sup>Observed (raw) data. <sup>b</sup>Multiple linear regression adjusted for age, gender and baseline insomnia severity (using Insomnia Severity Index score (Bastien et al., 2001)). <sup>c</sup>Least square mean for change from baseline to six month score. <sup>d</sup>Least square mean difference for change from baseline to six months score between sleep restriction and control group. <sup>e</sup>Unadjusted effect size = (mean observed difference sleep restriction group – mean observed difference control group)/pooled standard deviation of the mean observed differences. <sup>f</sup>PHQ-9 = Patient Health Questionnaire-9 (Kroenke et al., 2001). <sup>g</sup>GAD-7 = Generalized Anxiety Disorders-7 (R.L. Spitzer et al., 2006).

## 4.5.2 Primary outcomes

Summary results for the primary outcomes are shown in Table 4-5 and Table 4-6. Results for the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989), Insomnia Severity Index (ISI) (Bastien et al., 2001) and sleep efficiency are discussed in this section along with an interpretation of clinical meaningfulness using categorical treatment outcome and insomnia diagnosis.

### **Pittsburgh Sleep Quality Index**

After controlling for age, gender and severity of insomnia (using baseline ISS score), the adjusted difference in the mean change in PSQI score between the simplified sleep restriction and the control group was -2.14 (95% CI [-3.15, -1.13],  $p < 0.001$ ). A sensitivity analysis controlling for hypnotic use at six months yielded a similar pattern of significant results (adjusted difference = -1.56; 95% CI [-2.51, 0.61],  $p = 0.002$ ). Complete case sensitivity analysis (controlling for hypnotic use at six months) again produced a similar pattern of significant results (adjusted difference = -1.59; 95% CI [-2.55, 0.63],  $p = 0.002$ ). These results suggested that the simplified sleep restriction intervention was more effective than the control intervention in improving PSQI score.

### **Insomnia Severity Index**

After controlling for age, gender and severity of insomnia (using baseline ISS score), the adjusted difference in the mean change in ISI score between the simplified sleep restriction and the control group was -2.50 (95% CI [-3.97, -1.03],  $p < 0.001$ ). A sensitivity analysis controlling for hypnotic use at six months yielded a similar pattern of significant results (adjusted difference = -2.02; 95% CI [-3.45, -0.60],  $p = 0.006$ ). Complete case sensitivity analysis (controlling for hypnotic use at six months) also produced a similar pattern of significant results (adjusted difference = -2.08; 95% CI [-3.51, 0.66],  $p = 0.005$ ). These results suggested that the simplified sleep restriction intervention was more effective than the control intervention in improving ISI score.

### **Sleep efficiency**

Table 4-6 shows the means, change scores, and overall adjusted difference in sleep efficiency (SE) between the simplified sleep restriction and control groups. Sleep efficiency was measured using both sleep diary and actigraphy data. The results of the descriptive statistics for both observed and adjusted data are presented below.

### ***Sleep diary***

Using sleep diary data, both the sleep restriction group and the control group had an improvement in sleep efficiency over six months (6.72%; 95% CI [3.90, 9.54] vs 4.28%; 95% CI [1.86, 6.70]). After controlling for age, gender and severity of insomnia (using baseline ISS score), the adjusted least square mean difference for change in sleep diary sleep efficiency score between the sleep restriction and the control group was 2.44 (95% CI [-0.96, 5.84],  $p = 0.2$ ). There was no significant difference between the groups after controlling for hypnotic use at six months (adjusted difference = 1.22; 95% CI [-2.23, 4.66],  $p = 0.5$ ). These results suggested that there was no significant difference in the change in sleep diary sleep efficiency score between the simplified sleep restriction group and the control group.

### ***Actigraphy***

Using actigraphy data, the simplified sleep restriction group had a slightly increased sleep efficiency over six months (1.75%; 95% CI [0.42, 3.09]) but the control group had a slight reduction in sleep efficiency (-0.46%; 95% CI [-1.58, 0.65]). After controlling for age, gender and severity of insomnia (using baseline ISS score), the adjusted least square mean difference for change in sleep efficiency score measured by actigraphy between the simplified sleep restriction and the control group was 2.22 (95% CI [0.65, 3.79],  $p = 0.006$ ). Results were similar after controlling for hypnotic use at six months (adjusted difference 2.10; 95% CI [0.46, 3.74],  $p = 0.01$ ). These results suggested that there was a significant difference in the change in sleep efficiency between the simplified sleep restriction group and the control group when measured by actigraphy.

### **Clinical significance**

#### ***Categorical treatment outcomes***

For analysis of the categorical treatment outcomes participants were categorised into one of four treatment outcomes: response, remission, partial remission, or non-response. The change in PSQI score and sleep efficiency (%) were used to categorise the outcomes as previously described in Section 3.10. The proportion of participants in each group experiencing each treatment outcome are shown in Figure 4-8.

After controlling for age, gender and severity of insomnia (using baseline ISS score), ordinal regression for a multinomial distribution was performed to generate an odds ratio (OR = 3; 95% CI [1.3, 6.8],  $p = 0.008$ ). This suggested that those in the simplified sleep restriction group were three times more likely to have a favourable treatment outcome than those in the control group.

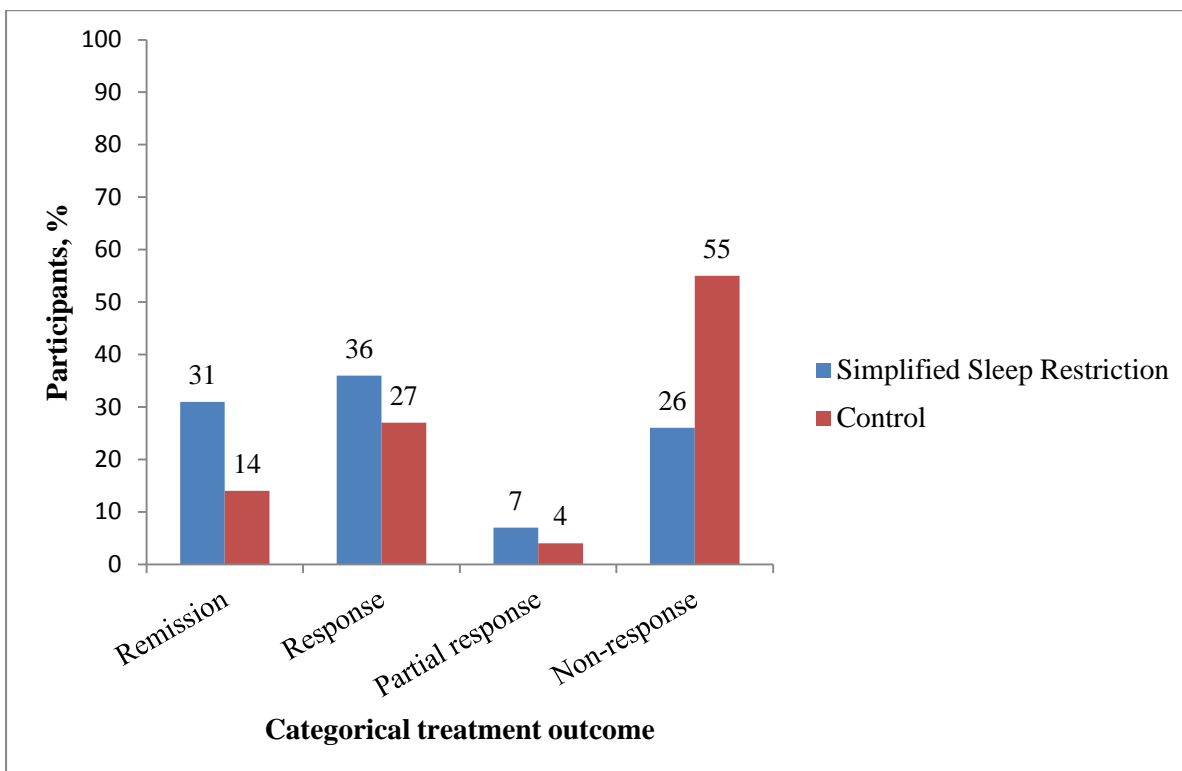


Figure 4-8: Categorical treatment outcomes for the ReFReSH trial at six months – four categories.

Outcomes for participants in the simplified sleep restriction (n = 42) and control groups (n = 49) ( $\chi^2 = 8.39$ ,  $p = 0.04$ ). Only those with complete PSQI and sleep diary data at follow up are included. The four categorical outcomes are based on those used by Buysse et al (Buysse et al., 2011). Categories relate to change in PSQI and sleep efficiency scores, and overall sleep efficiency percentage.

The categorical treatment responses were then collapsed into two categories creating a binomial outcome of remission or response versus partial response or non-response. The absolute improvement over time was 26% (95% CI [6.0%, 46%]), more with simplified sleep restriction than control. In other words, 67% experienced insomnia remission or treatment response in the simplified sleep restriction group compared with 41% in the control group. Therefore, simplified sleep restriction has a number needed to treat (NNT) of 4 (95% CI [2, 19]) to achieve a significant treatment response or remission of insomnia, compared with sleep hygiene advice alone (control).

After controlling for age, gender and severity of insomnia (using baseline ISS score), a logistic regression was performed to generate an odds ratio (OR = 2.7; 95% CI [1.1, 6.5],  $p = 0.03$ ). This suggested that those in the simplified sleep restriction group were 2.7 times more likely to have an insomnia remission or treatment response than those in the control group.

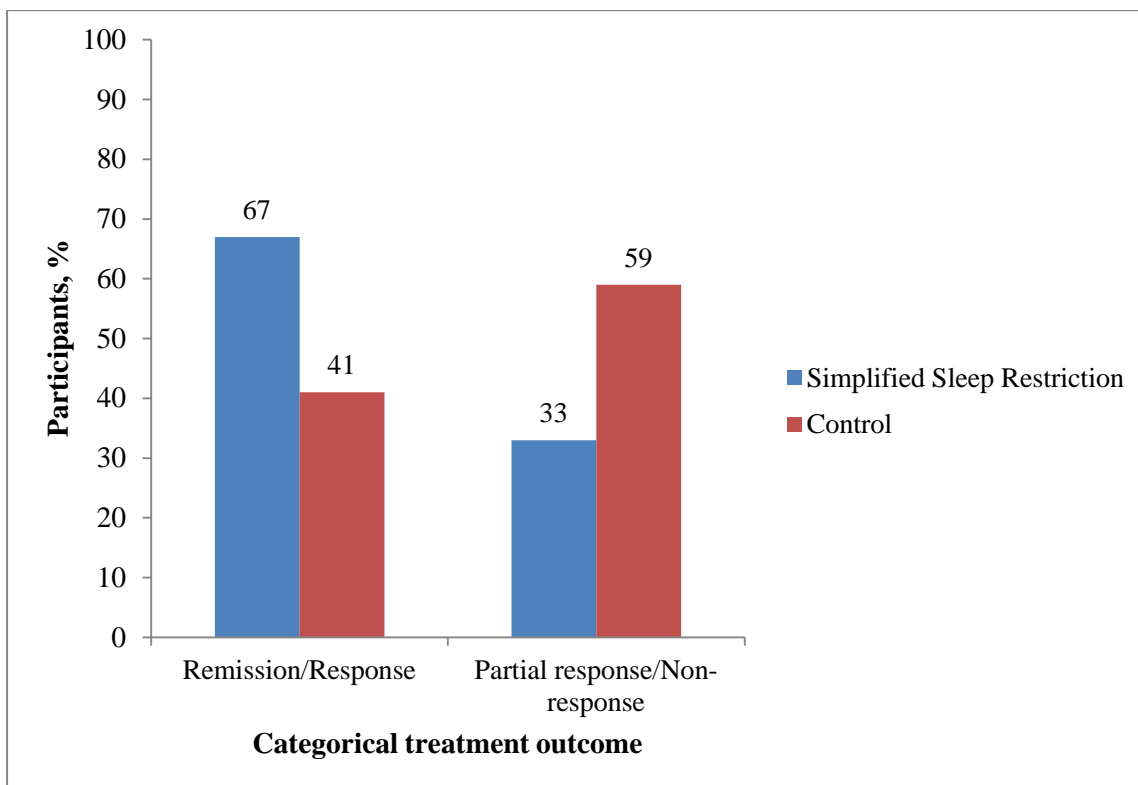


Figure 4-9: Treatment response to simplified sleep restriction compared to control over six months in the ReFReSH trial.

Outcomes for participants in the simplified sleep restriction ( $n = 42$ ) and control groups ( $n = 49$ ) ( $\chi^2 = 6.06$ ,  $p = 0.01$ ). Only participants with complete PSQI and sleep diary data at follow up are included. The two categorical outcomes based on those used by Buysse et al (Buysse et al., 2011). Categories relate to change in PSQI and sleep efficiency scores, and overall sleep efficiency percentage.

### ***Insomnia diagnosis***

However, the difference between the simplified sleep restriction group and the control group in the proportion of participants no longer meeting insomnia criteria did not meet statistical significance at either three months (64% [29/45] vs 45% [22/49];  $\chi^2 = 3.61$ ,  $p = 0.06$ ) or six months (84% [36/43] vs 66% [33/50];  $\chi^2 = 3.79$ ,  $p = 0.05$ ) using the *International Classification of Sleep Disorders (Second Edition)* (ICSD-2) general criteria for insomnia (American Sleep Disorders Association, 2005).

### **4.5.3 Secondary outcomes**

Tables 4-7 to 4-9 show the data for sleepiness, fatigue, sleep measures, depression and anxiety. The descriptive statistics for adjusted data are presented below.

## **Sleepiness**

After controlling for age, gender and severity of insomnia (using baseline ISS score), the adjusted least square mean difference for change in ESS score between the simplified sleep restriction and the control group was -0.07 (95% CI [-1.40, 1.27],  $p = 0.9$ ). These results suggested that there was no significant difference in the magnitude of change experienced in the simplified sleep restriction and control groups.

## **Fatigue**

After controlling for age, gender and severity of insomnia (using baseline ISS score), the adjusted least square mean difference for change in Flinders Fatigue Scale (FFS) (Grasidar et al., 2007) score between the simplified sleep restriction group and the control group was -2.27 (95% CI [-4.42, -0.13],  $p = 0.04$ ). These results suggested that simplified sleep restriction produced a significantly greater reduction in fatigue at six months (as measured by the FFS) than control.

## **Sleep measures**

### ***Sleep onset latency***

After controlling for age, gender and severity of insomnia (using baseline ISS score), the adjusted least square mean difference for change in sleep diary sleep onset latency (SOL) between the simplified sleep restriction group and the control group was -3.45 (95% CI [-11.23, 4.32],  $p = 0.4$ ). The adjusted difference in change in SOL measured by actigraphy was -6.13 (95% CI [-11.82, -0.44],  $p = 0.04$ ). These results suggested that simplified sleep restriction produced a significantly greater reduction in SOL at six months than control when measured by actigraphy, but not when measured by sleep diary.

### ***Wake after sleep onset***

After controlling for age, gender and severity of insomnia (using baseline ISS score), the adjusted least square mean difference for change in sleep diary wake after sleep onset (WASO) at six months between the simplified sleep restriction and the control group was -5.76 minutes (95% CI [-17, 5.47],  $p = 0.3$ ). The adjusted difference in change in WASO measured by actigraphy was -3.08 minutes (95% CI [-8.35, 2.18],  $p = 0.2$ ). These results suggested there was no significant difference in the change in WASO at six months between the groups when measured by either sleep diary or actigraphy.

### ***Total sleep time***

After controlling for age, gender and severity of insomnia (using baseline ISS score), the adjusted least square mean difference for change in sleep diary total sleep time (TST) at six months between the simplified sleep restriction and the control group was 4.72 minutes (95% CI [-12.39, 21.83],  $p = 0.6$ ). The

adjusted difference in change in TST measured by actigraphy was 0.10 minutes (95% CI [-10.47, 10.67],  $p = 0.99$ ). These results suggested there was no significant difference in the change in TST at six months between the groups when measured by either sleep diary or actigraphy.

## **Depression**

Table 4-9 shows the results for depression as measured by the PHQ-9 score (Kroenke et al., 2001). There was a significant trend toward improvement in PHQ-9 score from baseline to six months in both the simplified sleep restriction group ( $t(42) = 4.14, p < 0.001$ ) and the control group ( $t(49) = 3.75, p < 0.001$ ). However, after controlling for age, gender and severity of insomnia (using baseline ISS score), the adjusted least square mean difference for change in PHQ-9 score at six months between the groups was not significant (-0.53; 95% CI [-1.77, 0.71],  $p = 0.4$ ). This suggested that there was no worsening in depression with the simplified sleep restriction intervention over time.

## **Anxiety**

Table 4-9 shows the results for anxiety as measured by the GAD-7 score (R.L. Spitzer et al., 2006). There was a significant trend toward improvement in GAD-7 score from baseline to six months in both the simplified sleep restriction group ( $t(42) = 4.38, p < 0.001$ ) and the control group ( $t(49) = 2.45, p = 0.018$ ). However, after controlling for age, gender and severity of insomnia (using baseline ISS score), the adjusted least square mean difference for change in GAD-7 score at six months between the sleep restriction and the control group was not significant (-0.92; 95% CI [-1.93, 0.10],  $p = 0.08$ ). This suggested that there was no worsening in anxiety with the simplified sleep restriction intervention over time but that there was no difference between the groups.

## **4.6 Harms**

### **4.6.1 Adverse events**

There was a very low incidence of adverse events throughout the trial. The study was not powered to assess as statistically significant, differences in rare adverse events, so statistical analysis was not carried out. However, there was no obvious difference between the groups over the course of the trial (Table 4-10). Of particular note was that those in the simplified sleep restriction group did not experience any injuries or motor vehicle accidents in the initial two weeks of the trial when mild sleep deprivation can occur.



Table 4-10: Adverse Events Experienced by Participants in the ReFRReSH Trial

|                                   | Baseline <sup>a</sup> |                          | Week three <sup>b</sup> |                          | Six months <sup>c</sup> |                          |
|-----------------------------------|-----------------------|--------------------------|-------------------------|--------------------------|-------------------------|--------------------------|
|                                   | SSR<br><i>n</i> = 46  | Control<br><i>n</i> = 51 | SSR<br><i>n</i> = 45    | Control<br><i>n</i> = 51 | SSR<br><i>n</i> = 43    | Control<br><i>n</i> = 48 |
| <b>Adverse event <i>n</i> (%)</b> |                       |                          |                         |                          |                         |                          |
| Motor vehicle accident            | 3 (7)                 | 4 (8)                    | 0                       | 1 (2)                    | 2 (5)                   | 5 (10)                   |
| Injury                            |                       |                          |                         |                          |                         |                          |
| Medical attention                 | 9 (20)                | 5 (10)                   | 0                       | 1 (2)                    | 4 (9)                   | 6 (13)                   |
| No medical attention              | 7 (15)                | 5 (10)                   | 0                       | 2 (4)                    | 2 (5)                   | 8 (17)                   |
| Worsening angina                  | 0                     | 0                        | 0                       | 1 (2)                    | 0                       | 0                        |
| Myocardial infarction             | 0                     | 0                        | 0                       | 0                        | 0                       | 0                        |
| Stroke                            | 0                     | 0                        | 0                       | 0                        | 0                       | 0                        |
| Hospitalisation                   | 3 <sup>d</sup> (7)    | 1 <sup>e</sup> (2)       | 0                       | 0                        | 3 <sup>f</sup> (7)      | 3 <sup>g</sup> (6)       |
| Sleepiness                        |                       |                          |                         |                          |                         |                          |
| Driving                           | 1(2)                  | 3 (6)                    | 1 (2)                   | 0                        | 0                       | 2 (4)                    |
| Childcare                         | 0                     | 3 (6)                    | 1 (2)                   | 0                        | 0                       | 0                        |

Note. SSR = simplified sleep restriction. <sup>a</sup>Baseline questionnaire asks about occurrence of adverse events over preceding six months. <sup>b</sup>Week three questionnaire asks about sleepiness in the preceding two weeks (i.e. from time of treatment initiation). <sup>c</sup>Six month questionnaires asks about sleepiness in the preceding six months (i.e. the duration of the trial). <sup>d</sup>Panic attack, faint, pacemaker insertion. <sup>e</sup>MRI -deafness and loss of balance. <sup>f</sup>Finger surgery, knee replacement, gallstones. <sup>g</sup>Broken arm, ankle surgery, pneumonia.

#### 4.6.2 Physiological effects

Table 4-11 shows the results for the systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR). There was no significant difference in the change in either SBP ( $t(89) = 0.66, p = 0.5$ ) or DBP ( $t(89) = -0.1, p = 0.9$ ) between the groups. However, there was a statistically significant change in the heart rate between the groups (4.54 beats per minute; 95% CI [0.81, 8.27],  $p = 0.02$ ), although baseline heart rate was higher in the control group.

Table 4-11: Physiological Measures Over Six Months in the ReFRReSH Trial

|                                | Simplified sleep restriction                            |  |                                       | Control   |  |                                       | Difference between groups, [95% CI], <i>p</i> value <sup>b</sup> |
|--------------------------------|---|--|---------------------------------------|---|--|---------------------------------------|--|
|                                | Baseline score, mean (SE) <sup>a</sup><br><i>n</i> = 46 | Six month score, mean (SE) <sup>a</sup><br><i>n</i> = 43 | Mean difference [95% CI] <sup>b</sup> | Baseline score, mean (SE) <sup>a</sup><br><i>n</i> = 51 | Six month score, mean (SE) <sup>a</sup><br><i>n</i> = 49 | Mean difference [95% CI] <sup>b</sup> |  |
| <b>Physiological measure</b>   |   |  |                                       |   |  |                                       |  |
| Systolic blood pressure, mmHg  | 122.24 (2.06)   | 121.21 (2.15)  | -1.33 [-4.28, 1.63]                   | 123.88 (1.87) <sup>c</sup>                              | 125.06 (1.97)  | 0.25 [-3.48, 3.98] <sup>d</sup>       | -1.58, [-6.34, 3.19]<br>0.5                                      |
| Diastolic blood pressure, mmHg | 75.52 (1.53)  | 74.51 (1.42)   | -1.30 [-3.29, 0.68]                   | 75.62 (1.27)  | 74.92 (1.48)   | -1.46 [-3.97, 1.05] <sup>d</sup>      | 0.16, [-3.05, 3.37]<br>0.9                                       |
| Heart rate, beats per minute   | 68.91 (1.45)  | 69.47 (1.57)   | 0.72 [-1.98, 3.43]                    | 73.29 (1.52)  | 69.61 (1.37)   | -3.82 [-6.45, -1.19] <sup>e</sup>     | 4.54, [0.81, 8.27]<br><b>0.02</b>                                |

Note. <sup>a</sup>Observed (raw) data. <sup>b</sup>Calculated from t test procedure in SAS. <sup>c</sup>*n* = 50 due to machine error. <sup>d</sup>*n* = 48. <sup>e</sup>*n* = 49.

## **4.7 Meta-Analysis Including the ReFReSH Trial**

The six month observed data from the ReFReSH trial were added to the meta-analysis previously performed (see Section 2.3). Using sleep quality measured by the Pittsburgh Sleep Quality Index (Buysse et al., 1989) resulted in a significant difference between the sleep restriction group and the control group (Figure 4-10). Using sleep quality measured by the Insomnia Severity Index (Bastien et al., 2001) also resulted in a significant difference being shown between the groups (Figure 4-11). Without the contribution of the data from the ReFReSH study, there was no significant difference in sleep quality between the sleep restriction and control groups.

Combining the ReFReSH trial observed data for the sleep parameters, sleepiness, and fatigue did not result in any other overall changes in significance of results.

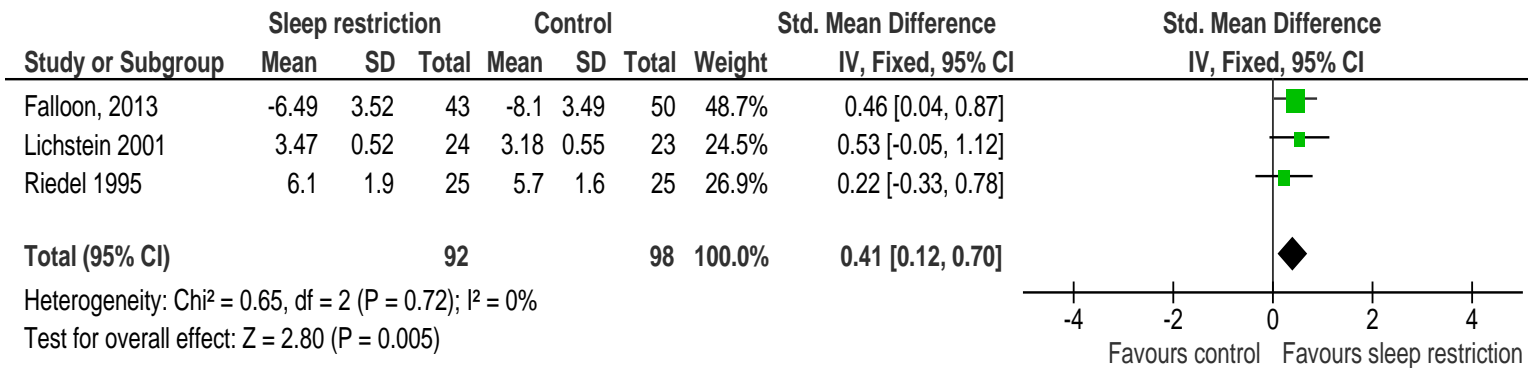


Figure 4-10: Meta-analysis comparing sleep quality at follow up between sleep restriction and control including ReFR<sub>e</sub>SH trial Pittsburgh Sleep Quality Index data<sup>a</sup>

<sup>a</sup>(Buysse et al., 1989)

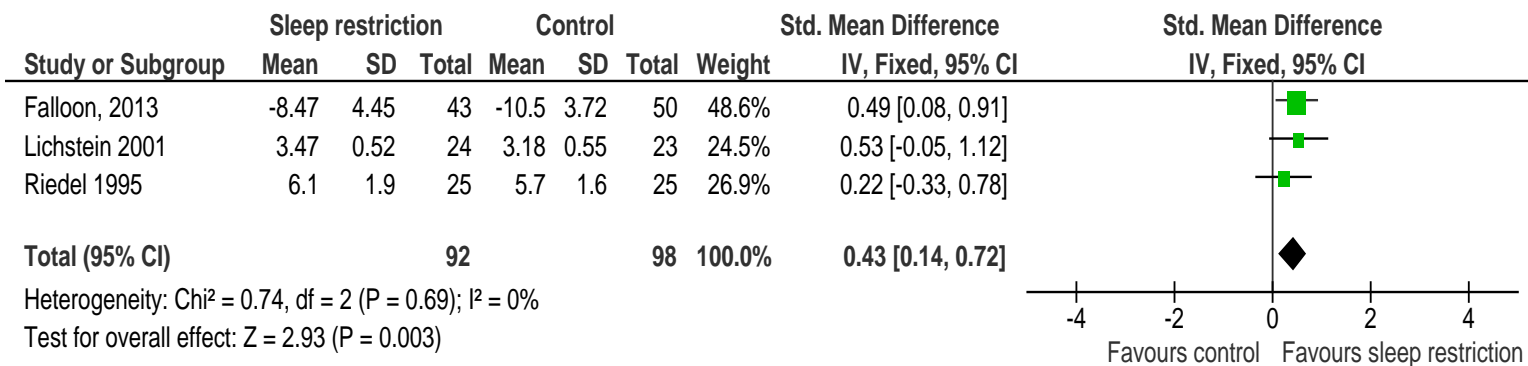


Figure 4-11: Meta-analysis comparing sleep quality at follow up between sleep restriction and control including ReFR<sub>e</sub>SH trial Insomnia Severity Index data<sup>a</sup>

<sup>a</sup>(Bastien et al., 2001)

## **4.8 Data Collection and Management**

Data were entered into the ACCESS database by both the author and a blinded research assistant (KS). The COMPARE procedure in SAS was run by an independent statistician (Simon Moyes) to check for differing values. The error rate was 0.01% with most discrepancies due to minor variation such as rounding incompatibilities. All errors were cross checked and the correct values entered. Subsequent COMPARE analysis was 100% correct.

A two week sample of sleep diary data was double analysed by a blinded research assistant (KS) for approximately twenty percent of participants, randomly selected. The error rate in this sample was used to determine if the sleep dairies for all participants needed to be double analysed. The overall error rate of the sample was 0.037%. This correlated with a difference in sleep efficiency scores of 0.04%, no change in SOL scores, a difference in WASO scores of 0.56 minutes and a difference in TST of 0.84 minutes. These rates of minor errors (due to rounding differences and handwriting interpretation) were accepted as being below the pre-set threshold (error rate of 0.05%) and no further double analysis was carried out.

## **4.9 Summary**

The randomised controlled trial of simplified sleep restriction as a treatment for primary insomnia in the primary care setting achieved high levels of follow-up at six months (97% of participants). The trial demonstrated significant improvements in the primary outcomes of sleep quality measured by the Pittsburgh Sleep Quality Index (Buysse et al., 1989) and the Insomnia Severity Index (Bastien et al., 2001), and sleep efficiency (measured by actigraphy) over six months, in the simplified sleep restriction group compared with the control group. The improvements in sleep quality seen in the simplified sleep restriction group were of a magnitude to be considered clinically meaningful. As well as this, the simplified sleep restriction group experienced a significant reduction in fatigue and sleep onset latency at six months compared with the control group. There was also a trend towards decreased sleepiness and reduced wake time after sleep onset. There was no evidence of adverse effects of the intervention including no worsening in depression and anxiety scores. Sensitivity analyses conducted to account for hypnotic use at six months and to explore complete case analysis made little difference to the results. The results and their implications are discussed further in Chapter 5.

## Chapter 5 Discussion

### 5.1 Main Findings

The first part of this thesis summarised the literature about insomnia. This demonstrated that insomnia was a prevalent condition in both the community and primary care settings. An association was shown between insomnia and medical conditions such as depression, anxiety, cardiovascular disease, and the metabolic syndrome. In addition, insomnia was shown to have a significant impact on general wellbeing, social functioning, and vocational functioning. The general practitioner was the health professional most likely to be consulted with a complaint of insomnia. Despite this, general practitioners had only a limited knowledge about insomnia treatments and there was a lack of available evidence for the effective management of insomnia in the primary care setting.

A systematic review of randomised trials of sleep restriction in primary insomnia found evidence for some improved sleep parameters, using meta-analyses. However, there was insufficient evidence to demonstrate overall improved sleep quality or efficiency. There was also a lack of evidence for a brief form of sleep restriction that could be delivered by general practitioners in the context of usual or slightly extended visit times. Therefore, more evidence was required, especially within the primary care environment. Furthermore, there was also insufficient evidence around potential harms of the intervention to draw conclusions.

The aims of the ReFRReSH randomised controlled trial were firstly, to evaluate the effectiveness of simplified sleep restriction for the treatment of primary insomnia in the primary care setting and, secondly, to identify any harms or safety concerns that may be attributed to the sleep restriction intervention. Significant improvements were demonstrated in sleep quality measured by the Pittsburgh Sleep Quality Index (Buysse et al., 1989), the Insomnia Severity Index (Bastien et al., 2001), and sleep efficiency (measured by actigraphy) over six months, in the simplified sleep restriction group compared to the control group. However, there was no significant difference between the simplified sleep restriction group and the control group in sleep efficiency measured by sleep diary. The clinical meaningfulness of the results was demonstrated with 67% in the simplified sleep restriction group experiencing insomnia remission or treatment response at six months compared to 41% in the control group. This corresponded to a number needed to treat of 4 (95% CI [2, 19]). The adjusted odds of getting an insomnia remission or treatment response for those in the simplified sleep restriction group was 2.7 times more likely than for those in the control group. Further support for the effectiveness of

simplified sleep restriction in treating primary insomnia is shown by the significant reduction in fatigue score at six months compared to the control group.

Inconsistent results or no significant difference in change between groups were found for the sleep measures of sleep onset latency, wake after sleep onset and total sleep time. In regards to the second hypothesis, no evidence was found that the simplified sleep restriction intervention led to any safety concerns. The reductions in the levels of depression and anxiety in the intervention group compared with the control group did not reach statistical significance, but these results were reassuring that the sleep restriction intervention did not cause increases in depression or anxiety scores. These findings are consistent with the findings in the literature regarding brief behavioural treatments leading to improvements in insomnia, as discussed below. When results were added to the meta-analyses conducted in the first part of the thesis, overall results now showed some improvements in sleep quality.

Therefore, this study has substantially added to the literature by showing that simplified sleep restriction is effective for adults with primary insomnia in a form that could be delivered in the primary care consultation. Furthermore, no significant harms associated with this intervention were observed during the trial.

## **5.2 How the Findings Relate to Previous Research**

One assumption underlying this research was that primary insomnia needs to be treated effectively in the primary care setting. To reflect this context, when considering the effectiveness of simplified sleep restriction, the results of the ReFReSH trial can be compared with the existing literature in three ways. Firstly, with the results of the pilot trial; secondly, with other studies using sleep restriction as a single-component treatment for primary insomnia; and lastly, compared to other non-pharmacological treatments for primary insomnia that have been designed for the primary care setting. These comparisons are discussed in turn below.

### **5.2.1 Comparison with the simplified sleep restriction pilot trial**

The current study yielded slightly lower treatment response rates than seen in the pilot trial (absolute benefit 26%, 95% CI [6, 46]; NNT 4, 95% CI [2,19] vs 38%, 95% CI [8.8, 59]; NNT 3, 95% CI [2,11], respectively) (Fernando et al., 2013). This may have been due to the outcomes measures being limited to a five-response Likert-type scale in the pilot, which had not been validated previously, or a lack of adjustment for possible confounding variables in the pilot. It may also have been due to the fact that the

“pilot” involved respondents to an advertisement in the paper, which may have included participants who were more motivated than those routinely screened for in general practices.

### **5.2.2 Comparison with single-component sleep restriction trials**

The current trial is a briefer treatment than used in the three other single-component sleep restriction trials analysed in the meta-analysis in Section 2.3 (L. Friedman et al., 2000; Lichstein et al., 2001; Riedel et al., 1995). The ReFRReSH trial also had 6 months follow-up compared with a maximum of 3 months amongst two previous trials and 12 months follow-up in the trial by Lichstein et al. (2001). The ReFRReSH trial also focussed more on the clinical meaningfulness and potential harms. It also demonstrated a statistically significant difference in sleep quality change scores, which was not shown in the other trials. However, a meta-analysis of the three other studies showed a statistically significant improvement in wake after sleep onset in the sleep restriction groups, whereas this was not demonstrated in the ReFRReSH trial. Levels of fatigue were significantly improved in the current trial, whereas this was not shown in the study by Lichstein et al. (2001), which was the only other study to use fatigue as an outcome.

### **5.2.3 Comparison with non-pharmacological treatments designed for primary care**

There are several trials of brief treatments for insomnia that have been designed for implementation in the primary care setting. Edinger and Sampson (2003) investigated an abbreviated form of CBT-I consisting of sleep education, stimulus control therapy and sleep restriction therapy compared with sleep education and sleep hygiene. Participants attended two individual sessions and were followed up after three months. Espie et al. (2007) compared CBT-I delivered by nurses in the primary care setting with treatment as usual. Participants attended five group sessions and were followed up after six months.

The study by Edinger and Sampson (2003) of abbreviated CBT-I was the most similar to the ReFRReSH trial in terms of intervention duration and intensity (two 25 minute sessions). The study showed statistically significant improvements compared to control in awakenings after sleep onset and sleep efficiency measured by sleep diaries as well insomnia symptoms measured by the Insomnia Symptom Questionnaire (Spielman, Saskin, et al., 1987). However, this was a small study ( $n = 20$ ) and, in contrast to most other insomnia research trials, consisted mostly of men (90%), which may limit the generalisability of their findings.

Buysse et al. (2011) compared sleep restriction therapy plus stimulus control (BBTI) to an information control. Participants attended two individual sessions and have two telephone follow ups. Both the ReFRReSH trial and the study by Buysse et al. (2011) used the Pittsburgh Sleep Quality Index as an



outcome (Buysse et al., 1989). However, it is difficult to compare the difference in effect of the two studies due to the time of outcome measurement (six months versus four weeks). The effect size of the improvement in PSQI score at six months in the ReFReSH trial was large (0.54). This compares with a large effect size seen in the study by Buysse et al. at six weeks (1.10). It is not possible to determine if the lower treatment effect seen in the ReFReSH trial was due to the earlier outcome measurement, or because BBTI is a more effective treatment. The six month categorical treatment response and remission rates of those in the sleep restriction intervention group in the current study (36% and 31%, respectively) appear slightly lower than those found using BBTI (44% and 40%, respectively) (Buysse et al., 2011). However, in the Buysse study only 60% of those in the BBTI group completed a six month follow up and the control group was not followed up past the primary analysis at one month. Therefore, it was not possible to determine if there was a statistically significant difference in treatment response in these groups at six months.

The proportion of participants no longer meeting criteria for insomnia at follow up was 84% in the ReFReSH study, higher than both that seen in the Buysse study (64%) and that seen with either CBT, pharmacotherapy, or a combination (78%, 56%, 75%, respectively) in a study of CBT based at a hospital sleep center (Buysse et al., 2011; Morin et al., 1999). It is interesting to note that the proportion of participants in the control group with no insomnia at follow up was 66% in the ReFReSH study compared with 12% in the Buysse study and 14% in the Morin study. This may suggest that the control group receiving personalised instructions (e.g. to reduce caffeine) during two sessions with the investigator rather than simply reading a handout out was actually an effective means of behaviour modification (and thus, a poorer control). In the ReFReSH trial the sleep hygiene instructions may have been adhered to strongly, whereas those in the simplified sleep restriction group may have paid more attention to the behavioural change required in the sleep schedule rather than the sleep hygiene lifestyle modifications. Both Espie et al. (2007) and Buysse et al. (2011) did not have control conditions designed to account for the effect of the face-to-face sessions with investigators (Buysse et al., 2011). In this situation, it is not possible to determine if the results seen were entirely due to the intervention being tested or if there was some other factor that influenced outcomes (for example, talking to an investigator and being part of a study).

In contrast to previous studies, the ReFReSH trial demonstrated statistically significant improvement compared with control on the sleep parameters of sleep efficiency and sleep onset latency (measured by actigraphy). Espie et al. (2007) only demonstrated statistically significant improvement compared to control in wake after sleep onset (measured by actigraphy) but not on any other measures. Edinger and Sampson (2003) only demonstrated statistically significant improvement compared to control in wake after sleep onset measured by sleep diary (actigraphy was not used in the study).

Direct comparison between studies is limited by the variation in outcome measures used and time points for follow up. However, it can be seen that changes in both self-reported sleep and objectively measured sleep are variable and are in some cases unchanged despite subjective improvements in sleep being reported (Lichstein et al., 2001). This corresponds to the findings in the ReFReSH trial and the improvement in subjective measures rather than sleep parameters may suggest that instead of indicating a lack of efficacy of the treatment, sleep parameters may be of lesser importance than the subjective measures of sleep quality, perceived insomnia severity, and indicators of daytime impairments. As stated by Moul, Hall, Pilkonis, and Buysse (2004), “self report data may report on sleep-related phenomena that are currently impossible to measure objectively with current technologies” (p. 178). Aikens and Rouse (2005) identified that patients especially seek help for insomnia if they perceive significant daytime impairments. They suggest that those who treat insomnia need to focus beyond “the numbers” of sleep improvement as some patients may be satisfied by an improved functional outcome even if their sleep is not perfectly normalised by treatment. When viewed from this perspective, the ReFReSH trial demonstrated that simplified sleep restriction was superior to control on all measures of importance - improved global sleep quality, reduced insomnia severity, and reduction in daytime fatigue.

## **5.3 Strengths and Limitations of the Study**

### **5.3.1 Intervention design**

Several novel components were developed and implemented in the sleep restriction intervention used in ReFReSH: the simplified sleep restriction script, the written sleep prescription, and the sleep self-adjustment algorithm. These components reflected the need to deliver the intervention from a primary care setting, to enhance participant engagement and motivation, and to have participants self-monitoring and adjusting their treatment. The inter-session interval of two weeks from the baseline appointment to the follow up after two weeks was designed to allow a balance between “therapist guidance and patient independence” where participants were able to implement behavioural changes and gain self-sufficiency in managing their sleep problem (Edinger, Wohlgemuth, Radtke, Coffman, & Carney, 2007, p.210).

### **5.3.2 Trial design**

The randomised controlled trial design was a major strength of the ReFReSH study. A further strength of the design was the incorporation of outcome measures that included sleep quality, sleep parameters, and measures of daytime functioning and mood. This was intended to identify meaningful and clinical relevant treatment effects, as well as using outcome measures that could be compared with the existing

literature and incorporated into future meta-analyses. The duration of follow up of participants was set as six months in order to balance the need to reflect medium-term durability of treatment effect with the practicalities of conducting a trial. The ReFReSH trial demonstrated a very low attrition rate of 3% suggesting that the treatments and the trial procedures were acceptable to participants.

However, recruitment to the trial may have been limited due to the stringency of the inclusion criteria. This was designed to ensure only those with primary insomnia were included in the trial. It was of particular importance to ensure the participants did not have high levels of depression or anxiety as it was unknown whether simplified sleep restriction would worsen these conditions. Future research investigating the effectiveness of simplified sleep restriction in a comorbid insomnia population would be valuable. That is, participants would meet the general criteria for insomnia, but would not be excluded on the basis of most other coexisting medical and psychiatric conditions.

### **5.3.3 Response rate**

The recruitment for the trial was slow and the response rate was low (Figure 4-2). This was partly due to the trial being conducted by the author on a part-time basis and over several years. However, the recruitment method itself also had some limitations. A mail out of 28,978 introductory letters yielded 2,740 responses (9.5%) from those who felt they had poor sleep and were interested in participating in the trial. In contrast, the New Zealand population prevalence of current or chronic sleeping problems has been estimated at 25% (Paine, Gander, Harris, & Reid, 2005). The local prevalence of “sleeping problems” in the primary care setting in Auckland, New Zealand, is estimated to be approximately 40% (Bruce Arroll et al., 2012). This would suggest that there were many people who may have met the general criteria for insomnia but were not interested in being part of a trial. Telephone follow up to the screening letter may have yielded a greater response; although this would have been very time-consuming. It is possible that people are not keen on receiving unsolicited mail, even if it is from their own general practitioner. For those who initially responded to the mail-out, there was a 55% response rate to the second questionnaire. The response rate may have been affected by people reading the study information and deciding they did not want to participate, or because of the perceived assessment burden of the 10 page questionnaire (which took 10 minutes to complete).

A future recruitment campaign might achieve a higher recruitment rate using a study website or social media; however this would recruit a general population rather than a primary care population. A possibility for primary care recruitment would be to send text information to those patients in practices already using such information technology for appointment reminders and recall messages.

### **5.3.4 Participants**

#### **Diagnosis**

No screening polysomnography or overnight monitoring was performed to provide objective screening for obstructive sleep apnoea or periodic limb movement disorders due to resource constraints. Despite questionnaire and clinical screening, it is possible that some participants in the trial may have had occult sleep apnoea, which would have confounded results, especially if those with sleep apnoea were distributed unevenly between groups. Insomnia and obstructive sleep apnoea frequently occur together (Luyster, Buysse, & Strollo, 2012). Previous studies have found about one-third of older adults screened by interview for primary insomnia were subsequently found to have at least moderate obstructive sleep apnoea on polysomnography (Lichstein, Riedel, Lester, & Aguillard, 1999; Lichstein et al., 2001). Buysse et al. (2011) found approximately 11% of their sample of interview-screened older adults had untreated obstructive sleep apnoea on polysomnography.

The ReFReSH trial adhered to research recommendations that state that assessing for the common clinical characteristics of obstructive sleep apnoea (high body mass index, increasing age, male, excessive daytime sleepiness, and loud snoring) by interview and excluding those who exhibit most of these characteristics is a reasonable approach to identify those with obstructive sleep apnoea (Buysse et al., 2006). In addition, the ReFReSH trial conducted a physical examination to further identify risk factors for obstructive sleep apnoea (for example, large neck or crowded airway), which may have excluded participants at risk for obstructive sleep apnoea that were not identified by questionnaire alone. Despite this, there may have been some participants in the ReFReSH trial who did not respond to simplified sleep restriction therapy due to the presence of obstructive sleep apnoea. This may have underestimated the true treatment effect of simplified sleep restriction.

#### **Participant characteristics**

The majority of participants in the ReFReSH trial were female (77%). This was to be expected as women have a higher risk of developing insomnia than men across all age groups (Ohayon, 2002). The predominance of females in the trial is also consistent with that seen in other similar studies (Buysse et al., 2011; Fernando et al., 2013; L. Friedman et al., 2000; Lichstein et al., 2001). There was a slight imbalance of gender between the simplified sleep restriction group (85% female) and the control group (71% female), which was most likely related to the relatively small sample size and the fact that the groups were not stratified on gender. The other baseline characteristics and sleep parameters were balanced suggesting adequate randomisation.

Almost all participants were New Zealand European which limits the generalisability of the results to other ethnic groups. The random selection of practices to be used as recruitment practices included two with predominantly low socioeconomic, ethnically diverse populations (and one with a predominantly Chinese population. However, there was an extremely low response rate from these practices and no participants recruited to the trial. This suggests that in order to conduct research in a low socioeconomic practice, or one with a high level of ethnic diversity (for example, Maori, Pacific Island, Chinese, and Refugee communities), a different approach may be necessary. Furthermore, the research location was a significant driving distance from some of the practices. If research assessments could have been conducted at participants' homes or local venues, this may have boosted recruitment in some areas. Language may well have been a significant barrier for some. The invitation letter from the general practitioner was in English, and may have included terms that were foreign to someone reading English as a second language.

The practicalities of childcare may also have been a barrier for others. Consideration of not only having a local venue, but giving the opportunity of childcare provided by the study would be a factor to consider for future studies. For example, a local church hall with crèche facilities available (hired by the researchers) and a day time drop-in policy rather than making appointments could be strategies to reach these populations more successfully. It could also be important to recruit and train research assistants either from the local community, or at least some who are familiar with the language and culture of the various ethnic groups. One general practice clinic was approximately one kilometre from the research centre at the Department of General Practice and Primary Health Care. Even this distance may have been a barrier to potential participants, as could have the barriers mentioned above. It is also possible that the additional stressors of life for some, for example in poorer socioeconomic communities, meant problems with sleep featured lower on the list of priorities.

### **5.3.5 Adequacy of randomisation**

Block randomisation was used in the ReFRReSH trial. A block size of six was chosen based on the estimated number of participants that may have been recruited from each general practice. This method of randomisation was used to ensure balance between the intervention and control group participants recruited from each practice (Efird, 2011). As the entry sequence into the study (the time of being recruited) was not thought to affect any participant characteristics, a zero intrablock correlation was assumed. Hence, no adjustment for randomisation blocks was performed. A disadvantage of block randomisation is that when the block size is known, the allocation of participants may be predictable, resulting in selection bias (Efird, 2011). The author was inadvertently aware of the block size in the ReFRReSH trial, due to involvement in the trial design. However, this knowledge was not thought to

cause selection bias due to the mail-out to all potentially eligible patients, and standard criteria used to establish final eligibility of each participant. In future, in order to reduce the possibility of selection bias, the investigator could be kept blind to block size, or a number of block sizes could be used that are randomly ordered, such as blocks of four, six, and eight.

Overall, baseline characteristics were balanced between the simplified sleep restriction group and the control group. This suggested the randomisation was adequate. No statistical testing for baseline differences was performed as this is not considered appropriate for randomised controlled trials (Senn, 1994). With correct randomisation, any baseline differences observed are likely be due to chance (Knol, Groenwold, & Grobbee, 2011). In the ReFReSH trial the only obvious imbalances noted in baseline characteristics between the groups were related to gender and sleeping medication use. This imbalance could create chance bias whereby imbalance between variables that may influence outcome can bias results (C. Roberts & Torgerson, 1999). However, gender was included as a confounding variable in statistical modeling and use of hypnotics was used in the sensitivity analysis to assess for any potential bias.

### **5.3.6 Outcome measures**

#### **Bias due to self-report**

Participants completed daily two week sleep diary recordings prior to baseline and six months. Participants were asked to complete these diaries daily, first thing in the morning. However, there was no validity check regarding the daily completion of these records. In a previous study daily phone-in of sleep diary information was used to ensure accurate daily recording (L. Friedman et al., 2000). However, most recent studies have not reported using a daily phone-in verification method (Buysse et al., 2011; Edinger & Sampson, 2003; Espie et al., 2007). Not using a daily verification method may have introduced a recall bias where sleep diary information may have been retrospectively recorded (rather than being recorded daily). However, any such recall bias should have affected both groups equally. The change in average sleep diary parameters was also the outcome variable of interest, rather than absolute values. It has been suggested that recording “errors” tend to stay constant over time, which may lessen the effect of any recall bias on the results (Coates et al., 1982; Means et al., 2003).

#### **Lack of blinding**

It has been estimated that a lack of double blinding (where both the participants and the outcome evaluators are unaware of the “active” and “control” allocations) is associated with, on average, a 17% exaggeration in treatment effect (Schulz et al., 1995). However, Schulz et al. (1995) also state “blinding should be of greater importance to minimising bias for some outcomes than for others” (p. 412). Attempts were made to compensate for the lack of blinding of the outcome assessor using self-report

questionnaires and electronic displays of objective measures that were signed by the participants to verify their accuracy (Section 4.2).

However, the rapport built up between the author and the participants could have created a “Hawthorne Effect”. The Hawthorne effect refers to the situation where there is a reporting bias that occurs as participants have a desire to demonstrate a positive effect to comply with the perceived intent of the observer (Perlis, McCall, Jungquist, Pigeon, & Matteson, 2005; Wickstrom & Bendix, 2000). This may have affected the difference seen between the groups, if the Hawthorne effect influenced the outcomes in one group more than another.

### **Multiple outcome measures**

Multiple outcome measures are necessary in the evaluation of insomnia in order to reflect the quantitative (changes in sleep measures such as minutes awake overnight) and the qualitative (such as subjective experience of sleep quality and impact on daytime functioning) aspects of insomnia (Buysse et al., 2006). In fact, it has been suggested that to reduce the number of domains assessed as outcomes risks missing important aspects of the multidimensional nature of insomnia and sleep quality (Morin, 2003). However, using multiple outcome measures may risk detecting a statistically significant effect where there is no real effect (type I error) (Feise, 2002). Selection of a primary outcome and several secondary outcomes has been suggested as a way to avoid exaggerating the overall type I error rate (Zhang, Quan, Ng, & Stepanavage, 1997). As multiple outcome measures were necessary for the ReFRoSH trial, the primary outcome measure of sleep quality was pre-defined to try to follow this recommendation (Feise, 2002; Zhang et al., 1997).

### **Sleep diary and actigraphy**

The change in magnitude and direction of sleep parameter measures was not the same between the sleep diary and the actigraphy data in the current trial. This discrepancy has also been noted in previous studies (Buysse et al., 2011; Espie et al., 2007). In the current trial, the simplified sleep restriction group showed improved sleep efficiency from baseline to six months in both sleep diary and actigraphy recordings. In the control group, sleep diary showed an increase in sleep efficiency, whereas actigraphy showed a slight reduction in sleep efficiency. A similar trend in results was seen in the study by Buysse et al (Buysse et al., 2011). The data recorded on a sleep diary can be affected by recall bias and there is also some suggestion that the abnormal information and memory processing seen in those with insomnia can influence estimates of sleep and awake times (Perlis et al., 1997). On the other hand, actigraphy is essentially a motion sensor using “activity counts” to determine if a time period is to be coded as “sleep” or “wake”. So neither sleep diary nor actigraphy is the “perfect” representation of

sleep. As they are both determining if sleep or wake occurred using different methods (subjective recall or amount of motion sensed) the discrepancy between the data is quite possible.

### **Sleep quality and fatigue**

In the ReFRReSH trial, significant improvements were seen in the simplified sleep restriction group compared with the control group in the subjective measures of sleep quality, insomnia severity, and fatigue. This suggests that the improvement in sleep quality and insomnia symptoms seen in the simplified sleep restriction group was clinically significant enough to affect the daytime consequence of fatigue. The Pittsburgh Sleep Quality Index (Buysse et al., 1989) does not have a component measuring fatigue, although the Insomnia Severity Index (Bastien et al., 2001) does have one specific fatigue-related question. This suggests that the changes in sleep quality as measured by the Pittsburgh Sleep Quality Index are not solely due to the improvement in fatigue.

The fatigue scores achieved by the sleep restriction group after six months (mean 7.30; standard deviation 5.46) are similar to those found in the “good sleeper” control in the original validation study of the FFS (mean 6.22; standard deviation 4.55) (Grasidar et al., 2007). The improvement in fatigue seen also supports the notion that whatever underlying sleep process has been changed by simplified sleep restriction, it may have been one that improves part of the restorative function of sleep (rather than simply causing changes in the quantitative measures of sleep). For example, there is some evidence in the literature regarding the association of higher levels of proinflammatory cytokines in those with primary insomnia compared to good sleepers (Burgos et al., 2006; Vgontzas et al., 2002). Interleukin-6 (IL-6) and tumour necrosis factor (TNF) are “fatigue-inducing cytokines” which also stimulate the hypothalamic-pituitary-adrenal axis (Vgontzas et al., 2002). Vgontzas et al (2002) have shown that chronic insomnia is associated with a shift of IL-6 and TNF secretion from nighttime to daytime. They hypothesize that this shift, combined with hypersecretion of the arousal hormone cortisol, may explain the daytime fatigue and difficulty falling asleep seen in those with insomnia (Vgontzas et al., 2002).

A strength of the ReFRReSH trial was the measurement of fatigue as an outcome measure. It is possible to speculate that the improved sleep quality and associated reduction in fatigue seen with simplified sleep restriction may be associated with a normalisation of the proinflammatory cytokine secretion patterns (that is, a shift back to nighttime secretion). This association of improved sleep plus improved fatigue could be therefore hypothesized to provide evidence of a fundamental pathophysiological change occurring in those who experienced this symptom improvement. However, this hypothesis could only be confirmed by the measurement of proinflammatory cytokines in future studies of simplified sleep restriction.



## **Caffeine**

Although caffeine use was measured at baseline medical interview, it was not used as an outcome measure. This was due to the need to minimise the number of outcomes being measured. However, it is possible that a reduction in caffeine in response to the sleep hygiene instructions in the “good sleep guide” may explain some of the improvements in sleep seen in the control group. At baseline, the control group had a slightly higher mean daily caffeine intake than the simplified sleep restriction group (3.7 units versus 2.7 units). For those in the control group there were fewer instructions to follow. Therefore, the control group participants may have been highly motivated to eliminate caffeine. The subsequent reduction in caffeine may have reduced hyperarousal and led to improved sleep (Roehrs & Roth, 2008). The improvement in sleep from stopping caffeine was commented on anecdotally by two control participants: GMC\_100 and GMC\_097. Both of these participants had a treatment “response” and no longer met criteria for insomnia at six months. In future research, recording caffeine intake at baseline and follow up would enable caffeine use to be taken into account when analysing results.

## **Harms**

One of the stated aims of the ReFReSH trial was to identify any harms or safety concerns that may be attributed to the simplified sleep restriction intervention. Potential harms of an intervention involving sleep restriction include increased sleepiness and accidents related to mild sleep deprivation experienced at the start of treatment (Connor et al., 2002; Kyle et al., 2011). Participants in the ReFReSH trial were all aware of the possible harms associated with being involved in the trial due to the information handouts provided. The monitoring of safety and harms was a strength of the trial. As noted by Kyle et al. (2013) “adverse effects are almost never systematically recorded and/or reported in trials of psychological/behavioural treatments” (p. 4). No significant adverse events were identified however, a significant change in heart rate between the two groups was shown. These findings are discussed below.

The adverse events measured in the ReFReSH trial were: motor vehicle accidents, physical injuries (requiring medical attention/not requiring medical attention), worsening angina, heart attack, strokes/transient ischaemic attacks (TIAs), hospital admissions, and situations of potentially dangerous sleepiness (for example, whilst driving). Blood pressure and resting heart rate were also monitored. Data was collected at baseline, at week three, and at six months. The data collected at week three was intended to capture potential problems related to the effects of mild sleep deprivation in the first two weeks of simplified sleep restriction. There was only one incidence of sleepiness whilst driving and one incidence of sleepiness whilst performing childcare duties. The low number of adverse events experienced overall precluded accurate statistical analysis. However, recently published research

suggests that data collection may have occurred too early to identify the harms associated with simplified sleep restriction. Kyle et al. (2013) investigated whether sleep restriction therapy was associated with increased sleepiness and impaired performance. Participants received a traditional form of sleep restriction therapy where time in bed allowance was equal to mean total sleep duration a baseline with weekly adjustments made according to sleep efficiency achieved. The study demonstrated that sleepiness peaked at the end of two weeks of treatment but that reaction time and attentional lapses on psychomotor vigilance tests were poorest at the end of three weeks of treatment (Kyle et al., 2013), whereas the ReFReSH trial only measured these at the start of the third week. It is possible that the ReFReSH study measured harms related to the simplified sleep restriction intervention several days too early in order to capture the period of poorest psychomotor vigilance. On the other hand, it may be that simplified sleep restriction is a “gentler” version of sleep restriction therapy than more “traditional” models and therefore is not associated with significant reduction in psychomotor vigilance.

The results of the current trial showed a statistically significant change in the heart rate between the groups (4.5 beats per minute; 95% CI, 0.8 to 8.3;  $p = 0.02$ ). On closer inspection, it can be seen that the baseline heart rate was higher in the control group than in the simplified sleep restriction group (73 beats per minute versus 69 beats per minute). At six months, both groups had similar mean heart rates (70 beats per minute versus 69 beats per minute). Therefore, rather than the significant change seen in the heart rate representing an effect of the control intervention, it may be that this represents a phenomenon such as regression towards the mean (Haeckel & Wosniok, 2004; Perlis, McCall, et al., 2005). Regression towards the mean refers to “the likelihood that an outcome variable will show a significant change based on the severity of the initial baseline values” (Perlis, McCall, et al., 2005, p. 382). It can also be seen that the mean heart rate for the simplified sleep restriction group was unchanged from baseline to six months (69 beats per minute at both time points).

### **5.3.7 Analysis**

An intention to treat approach was used for the trial analysis. This represents a conservative approach to analysis which minimises the risk of a type 1 error (finding a significant result when one does not exist) (Fergusson et al., 2002). Therefore, the results shown are considered to be a conservative estimate of the treatment effect of simplified sleep restriction. A complete case sensitivity analysis was performed for the subjective primary outcomes using only those participants with no missing data. This analysis yielded similarly significant results suggesting that the results were reasonably robust.

Mixed model for repeated measures (MMRM) was chosen for the analysis for the primary outcomes with measures at three months and six months. With this method, all available data are used and no imputations are performed. MMRM is an appropriate statistical method to deal with repeated measures

with missing data and is considered superior to more traditional methods such as repeated measures ANOVA (Krueger & Tian, 2004). It is also considered to be more reliable and more statistically solid than other approaches such as using the last-observation-carried-forward approach (Lane, 2008; Molenberghs et al., 2004). The MMRM approach is unlikely to result in the serious misinterpretation of results as long as any drop outs are random and occur fairly equally between groups (Lane, 2008; Siddiqui, Hung, & O'Neill, 2009). The ReFReSH trial drop outs met this criteria, thus misinterpretation of the results from attrition bias was unlikely. Furthermore, MMRM is consistent with an intention to treat approach (Molenberghs et al., 2004).

No imputation of missing data was performed. There was a low rate of missing data (3%). The reasons for missing data were considered to be unrelated to the trial for all those with incomplete data except for the one participant in the control group who was unable to be contacted. The assumption was made that the missing data were missing at random and unrelated to the study variables meaning that the data from dropouts could be ignored without bias for the MMRM analysis.

### **5.3.8 Generalisability**

General practices were approached randomly (using random number tables) to participate in the trial recruitment. This gives a level of external validity to the trial. External validity relates to the ability to relate the finding to the general population (Steckler & McLeroy, 2008). However, the generalisability of the findings was limited by the stringent inclusion criteria meaning the findings of this trial relate only to those with primary insomnia. Despite this, the literature suggests that behavioral interventions for insomnia are effective in both the primary insomnia and comorbid insomnia populations (Buysse et al., 2011; Edinger et al., 2009; Espie et al., 2007). Therefore, simplified sleep restriction may also be effective in both these populations. However, this is an area for future research.

Despite a random general practice clinic sampling procedure which encompassed several practices with predominantly non-New Zealand European patients, the ethnic composition of the study was not reflective of the New Zealand population at the national level which has 65% New Zealand European, 14% Maori, 7% Pacific peoples, and 9% Asian nationally (Statistics New Zealand, 2013, 2006 Census figures). This may also limit generalisability of findings to groups under-represented in the trial. Data on socioeconomic status was not collected in this trial. If the participants were more likely to have been from a higher socioeconomic status and if those with higher socioeconomic status responded differently than those with lower socioeconomic status (for example, having better understanding of the algorithm or motivation for behavioural interventions) the generalisability of the trial to different socioeconomic groups would also be limited.

All those with insomnia from each of the recruitment practices had an opportunity to participate in the trial, so participants were not selected for their likelihood to comply. In a primary care study looking at the acceptability of behavioural treatments for insomnia, no demographic associations were found (Bluestein, Healey, & Rutledge, 2011). However, acceptance of behavioral treatments for insomnia was higher in those with high self-efficacy for sleep-inducing behavior and dysfunctional beliefs and attitudes about sleep (Bluestein et al., 2011). This suggests that those sufficiently concerned and motivated to participate in a university research trial may be those who are more accepting of behavioural treatments.

The trial participants ranged in age from 17 to 75 years old. Previous trials of sleep restriction have been limited to the older age group (Epstein et al., 2012; L. Friedman et al., 2000; Lichstein et al., 2001; Riedel et al., 1995). Therefore the results of the ReFRReSH trial suggests that sleep restriction may also be effective in younger adults as well.

The generalisability of the trial may have been limited by the author delivering the interventions. Although a script was followed for the delivery of both the simplified sleep restriction and sleep hygiene interventions, it is possible that the high level of enthusiasm displayed by the author for treating insomnia may have provided a motivating factor for participants that would not be present in the “real world” setting, leading to exaggerated treatment responses due to treatment adherence. On the other hand, if simplified sleep restriction was delivered by a patient’s own general practitioner, the doctor-patient relationship may provide an equivalent or higher level of motivation for patients. In the context of “patient-centered” care, the plan to treat insomnia with simplified sleep restriction may have been reached as a collaboration between the doctor and patient. This “buy-in” to the treatment plan may also be a motivating factor for patients to follow the simplified sleep restriction instructions in the real world. Thus, the enthusiasm of the author may have simulated the influence of the trusted doctor-patient relationship often present in the general practice setting.

Future research conducted at the general practice clinic level where the simplified sleep restriction intervention was delivered by usual general practitioners would improve the generalisability of the findings. Tailoring the recruitment and intervention procedures for non-New Zealand European populations would also be important for future research.

### **5.3.9 Treatment of non-responders**

It was beyond the scope to the present study to examine specific characteristics of the treatment of non-responders. However, it is hypothesised that this may be a subgroup with persistently high levels of arousal. The simplified sleep restriction intervention does theoretically address hyperarousal, but it is not a major or direct mechanism of action of the intervention. There was no specific outcome measure

of arousal to assess change in the level of arousal from baseline to follow up to test this hypothesis. There is a need to develop a measure of arousal for insomnia research. If persistent hyperarousal was identified to be present in those resistant to insomnia treatment, specific “add on” targeted interventions for hyperarousal could be prescribed. This may require a different theoretical construct than that used for the simplified sleep restriction intervention used in the ReFRReSH trial. For example, the social cognitive theory describes a “process in which personal factors, environmental factors, and human behaviour exert influence upon each other” (Rimer & Glanz, 2005, p. 19). This theory acknowledges the influence the wider social environment may have on insomnia. Interventions tailored to address hyperarousal using this theoretical model may include relaxation and stress reduction, nutrition, and exercise treatments. They may also include changes to the environment and workplace, or involve friends and family. Therefore, it would be important to describe who treatment non-responders are in order to create a step-wise, tailored intervention for insomnia.

## **5.4 Implications and Recommendations for Future Research**

The ReFRReSH trial has shown that simplified sleep restriction is an effective treatment for primary insomnia. It is an intervention suitable for implementation in the primary care setting, by the general practitioner (or practice nurse) at the point of care (during the consultation, or a slightly extended consultation). This may reduce some of the major barriers to the care of those with primary insomnia. There are several ways these barriers may be reduced: by increasing general practitioner knowledge and confidence when treating those with insomnia, providing an often preferred non-pharmacological treatment option for those with insomnia, and avoiding the additional time and cost of being referred elsewhere for insomnia treatment.

There are some with insomnia who do not experience a satisfactory improvement with simplified sleep restriction. As previously mentioned, these may be those with a strong “hyperarousal” mechanism for their insomnia. Other potential causes for treatment non-response include high levels of sleep anxiety or the presence of another unrecognised sleep disorder. A comprehensive management algorithm for insomnia for primary care would acknowledge these treatment non-responders and give alternative options. This is envisioned as being analogous to the algorithms used to treat depression in primary care (New Zealand Guidelines Group, 2008). Therefore, to extend the finding of the ReFRReSH trial it would be important to develop an “insomnia care pathway” where each treatment option has relevant (primary care) evidence of effectiveness. Evaluation of the use of the algorithm by general practitioners would then provide information regarding the effectiveness of the overall approach. Clear, concise

guidelines would not only increase general practitioners' knowledge and confidence with treating insomnia, it may also lead to an increase in screening, or case finding, for insomnia.

#### **5.4.1 Developing an “insomnia care pathway”**

The development of an evidence-based algorithm for the treatment of insomnia marries well with the concept of a “stepped care” approach to the management of insomnia as has been suggested by Espie (2009). A stepped care approach to patient management has been conceptualised as a pyramid (Espie, 2009). On the base of the pyramid high patient volume is managed using low intensity treatments, with smaller volumes of patients “stepping up” to higher levels based on need, with greater expertise in assessment and treatment occurring more towards the top level. The criteria for an “entry level” treatment in a stepped care approach has been described as a treatment that is readily accessible, provided at lowest cost, at least personal inconvenience to the patient, requiring the lowest treatment intensity, and requiring the least specialist time (Bower & Gilbody, 2005).

Integrating the work of the author and colleagues in developing a screening tool for insomnia (B. Arroll, Fernando, Falloon, Warman, & Goodyear-Smith, 2011), a preliminary concept for an algorithm for the treatment of insomnia in primary care is presented in Figure 5-1. In the algorithm, primary insomnia is initially managed with sleep hygiene and simplified sleep restriction (an evidence-based step). Those with inadequate responses at six week review receive an individualised “add-on” treatment depending on the dominant persistent complaint. These additional treatments require evidence for their effectiveness. The ethos of the algorithm is that “correcting” disorganised sleep (using sleep restriction) is a fundamental requirement for all who suffer from insomnia. The additional “steps” or treatments acknowledge the interplay of various influences in the pathophysiology of insomnia, and that these influences may be different between individuals. Thus, the algorithm provides a structured, but individually tailored treatment plan for insomnia. Based on the evidence from the ReFReSH trial, it is possible that up to two thirds of those with primary insomnia would experience insomnia treatment or remission using the “core” instructions (sleep hygiene and self-managed sleep restriction) alone. The additional benefit from the add-on treatments is yet to be determined. The algorithm acknowledges the difficulty of obtaining specialist assessment for insomnia and appropriately reserves this for resistant or severe cases. It also suggests behavioural treatments that are within the general practitioners skill set to deliver (management tools and additional notes regarding hypnotic use or withdrawal would be incorporated into the algorithm or the reverse of the algorithm card). The treatment approach is similar to that used for depression management in primary care which provides a guideline “at the fingertips” for the practitioner during a consultation (New Zealand Guidelines Group, 2008).

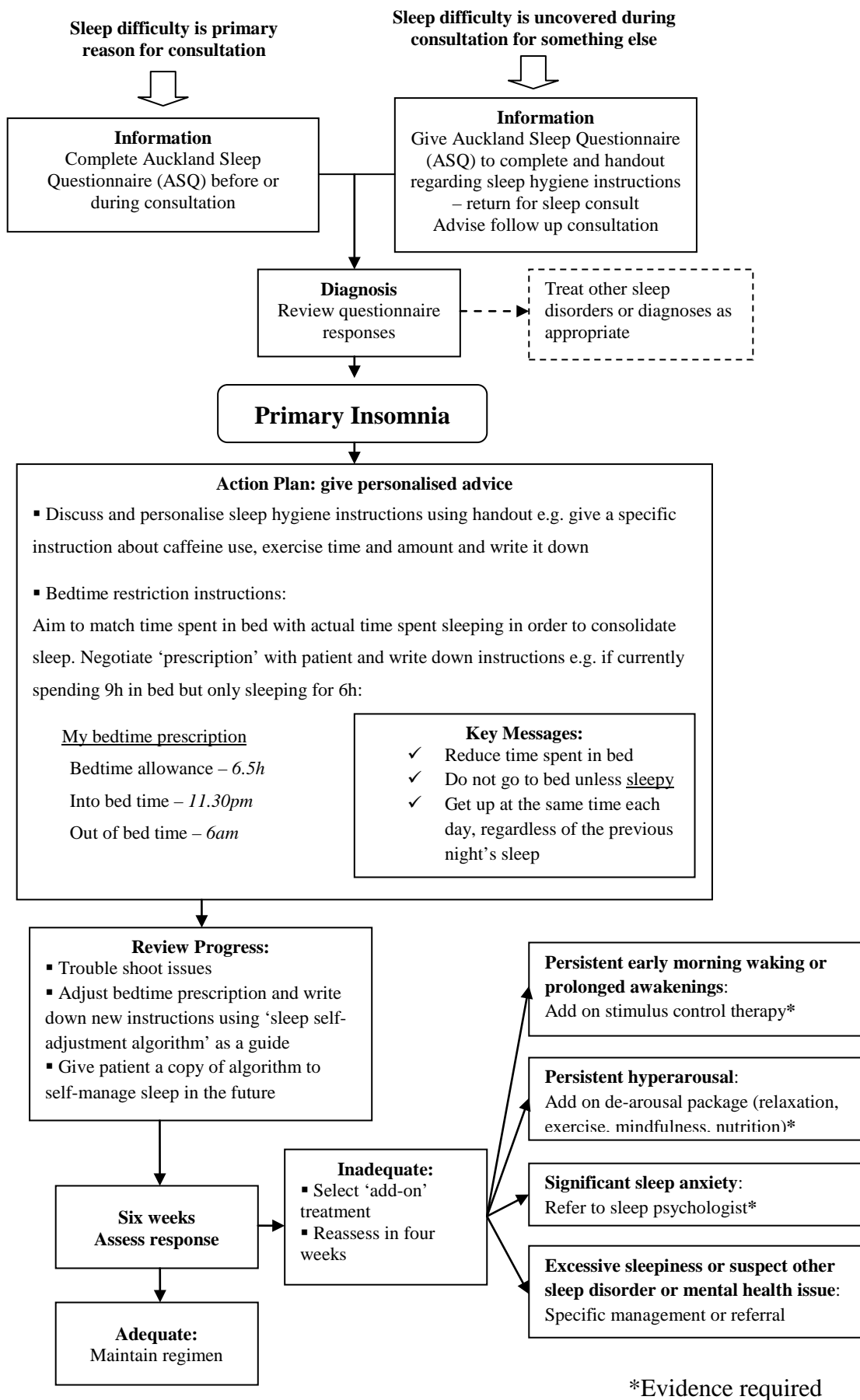


Figure 5-1: Provisional algorithm for the “stepwise” evidence-based treatment of primary insomnia in Primary Care

## **5.5 Conclusion**

The results of this study of simplified sleep restriction as a treatment for primary insomnia in the primary care setting suggest that it is an effective and safe treatment for primary insomnia that could be delivered at the “point-of-care” during a primary care consultation. This information has been incorporated into a proposed primary care treatment algorithm designed to educate general practitioners (and primary care nurses) regarding the management of insomnia. The results challenge the treatment paradigm that negative cognitions and dysfunctional sleep beliefs have a pre-eminent role in the causation and maintenance of insomnia thus necessitating specific psychological treatment aimed at those cognitions (as is the case with cognitive-behavioural therapy). An effective, purely behavioural treatment may be more acceptable to patients who are unwilling to pursue a “psychological” treatment and may be more acceptable to general practitioners to employ as a treatment option.

Furthermore, and perhaps most importantly, the evidence-based treatment model proposed as a consequence of the research project allows a much needed simplification of treatment options for primary insomnia in the primary care setting. The hope is that more general practitioners will feel confident in managing their patients with insomnia without needing medication as often and that more patients suffering from the affliction of chronic insomnia will achieve an acceptable improvement in symptoms or even remission of insomnia than might have previously. The next step is to evaluate the effectiveness of sleep restriction for those with comorbid insomnia. Further research should also evaluate the use of simplified sleep restriction in the context of the primary care treatment algorithm in the “real-world” setting in terms of acceptability and patient outcomes.



## Appendix A: Studies Included in the Systematic Review of Sleep Restriction for Insomnia

| Study          | RCT? | Primary insomnia or insomnia? | Adult, older adult or age ≥ 16 years old? | Insomnia diagnosed using standard criteria?                      | Exclusion of those with other sleep disorder or comorbid/secondary insomnia?   | Use of standardised outcome measure (e.g. PSQI), objective measure (e.g. PSG or actigraphy), or sleep diaries?   | Comments                 |
|----------------|------|-------------------------------|---|--|--|--|--------------------------|
| Fernando 2013  | Yes  | Yes                           | Yes<br>≥ 16 years old                     | Yes<br>DSM-IV_TR<br>Questionnaire then<br>face-to-face interview | Yes<br>Hospital Anxiety and<br>Depression Scale<br>(HADS) and Auckland<br>Sleep Questionnaire<br>version one (ASQ v1).   | No<br>Questioned about how<br>well they were sleeping:<br>'Much worse', 'worse',<br>'same', 'better' or<br>'much better'.                                | <b>Include in review</b> |
| Lichstein 2001 | Yes  | Yes                           | Yes<br>≥ 59 years<br>old                  | Yes<br>International<br>Classification of Sleep<br>Disorders     | Yes<br>Interview and self-<br>report<br>State-Trait Anxiety<br>Inventory (Anxiety)<br>Geriatric Depression<br>Scale<br>Mini Mental State<br>Exam<br>Cornell Medical Index<br>polysomnography | Yes<br>Insomnia Impact Scale<br>Beliefs and Attitudes<br>about Sleep Scale<br>Fatigue Severity Scale<br>2 week sleep diary<br>2 night<br>polysomnography | <b>Include in review</b> |

|               |     |     |                          |  |   |  |  |
|---------------|-----|-----|--------------------------|--|---|--|--|
| Friedman 2000 | Yes | Yes | Yes<br>≥ 55 years<br>old | Yes<br>International<br>Classification of Sleep<br>Disorders | Yes<br>Structured telephone<br>interview<br>Sleep disorders<br>questionnaire<br>Geriatric Depression<br>Scale<br>Folstein Mini Mental<br>states Exam<br>Structured Clinical<br>Interview for DSM-IV | Yes<br>Actigraphy<br>Sleep diary<br>Stanford Sleepiness<br>Scale | <b>Include in review</b><br>Sleep restriction therapy<br>Nap sleep restriction<br>therapy<br>Modified sleep hygiene<br>(control)<br><br>Didn't have any global<br>measures of sleep<br>quality   |
| Riedel 1995   | Yes | Yes | Yes<br>≥ 60 years        | Yes<br>DSM-III   | Yes<br>Interviews using<br>general health and sleep<br>questionnaires (not<br>named)  | Sleep diaries<br>Stanford Sleepiness<br>Scale                    | <b>Include in review</b><br>Would need to compare<br>education only group to<br>education plus guidance<br>to get a true idea of the<br>effectiveness of single<br>therapy SRT. However,<br>the video included<br>reference to restricting<br>time in bed. |

*Note.* Studies were included in the systematic review if they were randomised controlled trials.

## Appendix B: Studies Excluded From Systematic Review of Sleep Restriction for Primary Insomnia

| Study        | RCT? | Primary insomnia or insomnia? | Adult, older adult or age ≥ 16 years old? | Insomnia diagnosed using standard criteria?   | Exclusion of those with other sleep disorder or comorbid/secondary insomnia?  | Use of standardised outcome measure (e.g. PSQI), objective measure (e.g. PSG or actigraphy), or sleep diaries?               | Comments  |
|--------------|------|-------------------------------|---|---|---|--|---|
| Epstein 2012 | Yes  | Yes                           | Yes<br>≥ 55 years old                     | Yes<br>Two week sleep diary (≥45 minutes waking on ≥ 3 nights) and duration > 6 months and impaired daytime functioning | Yes<br>Brief Symptom Inventory<br>Mini Mental State Exam<br>Major physical or mental illness<br>Epworth Sleepiness Scale<br>Respiratory Disturbance Index<br>Participant and bedpartner interview | Yes<br>Sleep diaries<br>Actigraphy<br>Insomnia Severity Index<br>Geriatric Depression Scale<br>State-Trait Anxiety Inventory | Not eligible for review<br>Compared 4 group: SRT, SCT, SRT+SCT, wait list control.<br>However, all treatment groups also received sleep hygiene and sleep education (including cognitive strategies).<br>Therefore, not true single component comparison. |
| Kyle 2011    | No   | Yes                           | Yes<br>18-65 years old                    | Yes<br>Research diagnostic criteria for primary insomnia  | Yes<br>Glasgow Sleep Centre screening interview schedule  | Yes<br>Insomnia Severity Index<br>Pittsburgh Sleep   | Not eligible for review as it is an uncontrolled study  |

|               |    |     |                                       |    |  |   |  |
|---------------|----|-----|---------------------------------------|----|--|---|--|
|               |    |     |                                       |    |  | Quality Index<br>Glasgow Sleep Effort<br>Scale<br>Daytime functioning<br>questionnaires |  |
| Spielman 1987 | No | Yes | Unclear<br>Assumed<br>to be<br>adults | No | Yes<br>Medical history and<br>exam plus unstructured<br>interview<br>Polysomnography | Insomnia symptom<br>questionnaire:<br>'better', 'no different',<br>or 'worse'           | Not eligible for review<br>as not an RCT |

## Appendix C: Data Extraction Form

**Reviewer:**

**Review/revision date:**

|               |  |
|---------------|--|
| <b>Paper:</b> |  |
|---------------|--|

| Variable            | Questions to consider  | Adequate?<br>X/√/unclear |
|---------------------|--|--------------------------|
| Methods and setting | Study design: <i>RCT</i><br>Total study duration:<br>Sequence generation:<br>Allocation sequence concealment:<br>Other concerns about bias |                          |
| Participants        | Total number:<br>Setting:<br>Diagnostic criteria:<br>Age:<br>Sex:<br>Country:<br>Co-morbidity:<br>Ethnicity:                               |                          |

|                              |  |  |
|------------------------------|--|--|
|                              | Date of study:   |  |
| Intervention                 | Total number of intervention groups:<br>INTERVENTION<br>COMPARISON   |  |
| Outcome and time             | Outcomes and time points<br>1. Collected<br>2. Reported<br>For each outcome of interest:<br>Outcome definition, unit of measurement  |  |
| Results                      | Number of participants allocated to each intervention group<br>For each outcome of interest:<br>Sample size<br>Missing participants<br>Summary data for each intervention group<br>(2x2 for dichotomous; means and SD for continuous data)<br>Estimate of effect with confidence interval; P value |  |
| RAAMbo                       | Representative participant population?<br>Allocation (randomisation and allocation concealment adequate)?<br>Accounted (are all participants accounted for in groups and outcomes)?<br>Measurement – blind and/or objective?   |  |
| Intention-to treat analysis? | Was analysis performed in accordance with the principle of intention-to-treat?   |  |

|             |   |  |
|-------------|---|--|
| Confounding | Was there any adjustment for potential confounding? |  |
|-------------|---|--|

|                                      |  |
|--------------------------------------|--|
| <b>Overall assessment of quality</b> |  |
|--------------------------------------|--|

**Risk of Bias (www.cochrane-handbook.org)**

| <b>Domain</b>                          | <b>Judgement</b><br><i>Low risk, high risk, unclear risk</i> | <b>Support for judgement</b> |
|--|--|------------------------------|
| Adequate random sequence generation?   |  |                              |
| Allocation concealment?                |  |                              |
| Blinding? (participants and personnel) |  |                              |
| Blinding of outcome assessment?        |  |                              |
| Incomplete outcome data?               |  |                              |
| Selective reporting?                   |  |                              |
| Other bias?                            |  |                              |

|   |  |
|---|--|
| <b>Overall assessment of risk of bias</b> |  |
|---|--|

## Appendix D: Data Extraction Tables for Systematic Review of Sleep Restriction for Primary Insomnia

|                     |   |
|---------------------|---|
| Paper: Riedel, 1995 | Sleep Compression and Sleep Education for Older Insomniacs: Self-Help Versus Therapist Guidance |
|---------------------|---|

| Variable                                      | Questions to consider  | Adequate?<br>X/√/unclear |
|---|--|--------------------------|
| Methods and setting                           | Study design: <i>RCT (random assignment then last third of participants assigned to satisfy matching criteria on age and gender.</i> | √                        |
|   | Total study duration: <i>2 months (short-term)</i>   | √                        |
|   | Sequence generation:   | Unclear                  |
|   | Allocation sequence concealment  | Unclear                  |
|   | Blinding   | Unclear                  |
|   | Other concerns about bias  |                          |
| Participants                                  | Total number: <i>125 (75 insomniacs, 50 noninsomniacs)</i>   | √                        |
|   | Setting: <i>Community</i>  | √                        |
|   | Diagnostic criteria: <i>DSM-III</i>  |                          |
|   | Age: <i>≥ 60 years</i>   |                          |
|   | Sex: <i>Male (n=43) and female (n=82)</i>  |                          |
|   | Country: <i>USA</i>  |                          |
|   | Co-morbidity: <i>nil</i>   |                          |
|   | Socio-demographics: <i>not reported</i>  |                          |
|   | Ethnicity: <i>not reported</i>   |                          |
| Date of study: <i>unclear. Published 2001</i> |  |                          |



|                  |  |                   |
|------------------|--|-------------------|
| Intervention     | <p>Total number of intervention groups: 5</p> <p>INTERVENTION</p> <p>Specific intervention: <i>Video (insomniac group and non-insomniac group)</i></p> <p><i>'Sleep education for seniors' – ages-changes in sleep, recommends adopting age-appropriate sleep goals. Recommends restricting time in bed. Possible hazards of sleeping medication. Brochure outlining the main points of the video.</i></p> <p><i>Viewed at baseline and two weeks.</i></p> <p>INTERVENTION</p> <p>Specific intervention: <i>Video plus guidance (insomniac group and non-insomniac group)</i></p> <p><i>Video at session 1 plus specific sleep-compression treatment.</i></p> <p><i>Session 1: reduce excess TIB by 50%</i></p> <p><i>Session 2 reduce excess TIB by 25% of baseline difference</i></p> <p><i>Session 3: Video and reduce excess TIB by 25% of baseline difference</i></p> <p><i>Session 4: encouraged to maintain sleep schedule</i></p> <p>COMPARISON</p> <p><i>Specific intervention: wait list control</i></p> <p><i>Answered a week's worth of questionnaire at baseline, post treatment and 2 month follow up.</i></p> | <p>√</p> <p>√</p> |
| Outcome and time | <p>Outcomes and time points</p> <p>Collected</p> <p>Reported</p> <p><i>Baseline, post treatment, 2 month follow up</i></p> <p><i>SOL (mins)</i></p> <p><i>TST (mins)</i></p>   | <p>√</p>          |

|         |  |                            |
|---------|--|----------------------------|
|         | <p><i>TIB (mins)</i></p> <p><i>WASO (mins)</i></p> <p><i>SE (%)</i></p> <p><i>Stanford sleepiness scale</i></p> <p>Sleep satisfaction scale (1-10), Sleep knowledge quiz (0-9)</p>   |                            |
| Results | <p>Number of participants allocated to each intervention group</p> <p><i>Compare insomniac video and guidance with video only?</i></p> <p><i>25 in each group</i></p> <p>Missing participants: <i>nil</i></p> <p>Estimate of effect with confidence interval; P value:</p> <p><i>Means and SD presented. No confidence intervals. P&lt;0.05 for all outcomes comparing baseline to follow up (but no comparison of difference in change between groups in table)</i></p> <p><b>SOL:</b> “ <i>the analysis of simple effects for group revealed no significant differences between groups at pretreatment, post treatment or followup</i>”</p> <p><b>TST:</b> “<i>F test for group was non significant</i>”, “<i>no significant differences between groups at pretreatment and follow up</i>)”.</p> <p><b>WASO:</b> “<i>group effect non significant</i>” p59</p> <p><b>SE:</b> “<i>group effect was not significant</i>”</p> <p><b>Sleep satisfaction:</b> “<i>significant effect for group, time , and their interaction</i>”. “<i>Video plus guidance group significantly more satisfied with sleep at posttreatment than control group and this remained stable to follow up</i>”.</p> <p><b>Sleepiness:</b> “<i>significant main effect for time, but group and interaction effects were nonsignificant</i>”.</p> <p><b>Knowledge:</b> <i>reported but not required for SR</i></p> | <p>√</p> <p>√</p> <p>√</p> |

|                              |  |                                      |
|------------------------------|--|--------------------------------------|
| RAAMbo                       | Representative participant population?<br>Allocation (randomisation and allocation concealment adequate)?<br>Accounted (are all participants accounted for in groups and outcomes)?<br>Measurement – blind and/or objective? | Unclear<br>Unclear<br>Yes<br>Unclear |
| Intention-to treat analysis? | Was analysis performed in accordance with the principle of intention-to-treat?   | Yes                                  |
| Confounding                  | Was there any adjustment for potential confounding?  | No                                   |

|                                      |                    |
|--------------------------------------|--------------------|
| <b>Overall assessment of quality</b> | <b>Low quality</b> |
|--------------------------------------|--------------------|

### Risk of Bias ([www.cochrane-handbook.org](http://www.cochrane-handbook.org))

| <b>Domain</b>                          | <b>Judgement</b><br><i>Low risk, high risk, unclear risk</i> | <b>Support for judgement</b>  |
|--|--|---|
| Adequate random sequence generation?   | High risk  | <i>No description in text. Additional information from Lichstein qualified adequacy as “partial”.</i> |
| Allocation concealment?                | Unclear  | <i>No information available</i>   |
| Blinding? (participants and personnel) | High risk  | <i>No blinding (additional information from Lichstein who was co-author)</i>                          |
| Blinding of outcome assessment?        | High risk  | <i>No blinding (additional information from Lichstein who was co-author)</i>                          |
| Incomplete outcome data?               | Low risk   | <i>No attrition</i>   |
| Selective reporting?                   | Low risk   | <i>Outcomes reported as stated in paper. No registration of trial for confirmation though.</i>        |
| Other bias?                            |  |   |

|   |                |
|---|----------------|
| <b>Overall assessment of risk of bias</b> | <b>Unclear</b> |
|---|----------------|

|                       |  |
|-----------------------|--|
| Paper: Friedman, 2000 | An Actigraphic Comparison of Sleep Restriction and Sleep Hygiene Treatments for Insomnia in Older Adults |
|-----------------------|--|

| Variable            | Questions to consider   | Adequate?<br>X/√/unclear                        |
|---------------------|---|---|
| Methods and setting | <p>Study design: <i>RCT</i></p> <p>Total study duration: <i>4 week treatment, 3 month follow up</i></p> <p>Sequence generation:<br/><i>Modification of Efron procedure in subgroups stratified by TST and napping</i></p> <p>Allocation sequence concealment:</p> <p>Blinding: <i>therapists not blinded but blinded to objective outcome measures, don't know about outcome assessors</i></p> <p>Other concerns about bias</p> | <p>√</p> <p>√</p> <p>Unclear</p> <p>Unclear</p> |
| Participants        | <p>Total number: <i>39</i></p> <p>Setting: <i>Community</i></p> <p>Diagnostic criteria: <i>ICSD</i></p> <p>Age: <i>≥ 55 years old</i></p> <p>Sex: <i>male (n = 13), female (n = 26)</i></p> <p>Country: <i>USA</i></p> <p>Co-morbidity: <i>nil</i></p> <p>Ethnicity: <i>unknown</i></p> <p>Date of study: <i>published 2000</i></p>   | Small study                                     |

|                  |   |                   |
|------------------|---|-------------------|
| Intervention     | <p>Total number of intervention groups: 3</p> <p>Once a week for 4 weeks, total six meetings for all groups</p> <p>Groups had equal amount of therapist time</p> <p>INTERVENTION</p> <p><i>Sleep restriction plus sleep hygiene ***</i></p> <p><i>Weekly increments of TIB according to a fixed algorithm based on initial TST. YIB only increased by going to bed earlier. All subjects receive 7h TIB by the end of the 4<sup>th</sup> treatment week.</i></p> <p>INTERVENTION</p> <p><i>Sleep restriction with nap modification plus sleep hygiene***</i></p> <p>30 min daily afternoon nap between 1-3pm.</p> <p>COMPARISON</p> <p><i>Sleep hygiene</i></p> <p><i>Standard sleep hygiene modified so no instructions re napping or sleep scheduling but did include stimulus control instructions ***</i></p> | <p>√</p> <p>√</p> |
| Outcome and time | <p>Outcomes and time points</p> <ol style="list-style-type: none"> <li>1. Collected</li> <li>2. Reported</li> </ol> <p>Baseline, posttreatment (last 2 weeks of treatment), follow up (3mths after end of treatment)</p> <p>Outcome definition</p> <p>Actigraphic (sleep diary also available)</p> <p>TST (min)</p> <p>SE (%) TST/TIB (getting into bed-getting out of bed)</p>   | <p>√</p>          |

|         |   |   |
|---------|---|---|
|         | <p>SOL (min)</p> <p>WASO (min) calculated from TIB-TST</p> <p>Nb TWAK included in WASO</p> <p>Urine tox used to confirm participants were not taking sleeping medications</p>   |   |
| Results | <p>Number of participants allocated to each intervention group</p> <p><i>SRT n=16, NSRT n=12, HYG n=11</i></p> <p>For each outcome of interest:</p> <p>Sample size</p> <p><i>Sleep diary results: SRT n=16, NSRT n=12, HYG n=11</i></p> <p><i>Actigraphy results: SRT n=16, NSRT n=11, HYG n=10</i></p> <p>Missing participants – 10% attrition rate.</p> <p>Summary data for each intervention group</p> <p><i>See paper – means and SD</i></p> <p>Estimate of effect: P values no CI</p> <p><i>Note that primary outcome was actigraphy but the results were a mean of 2,3, or 4 nights actigraphy only</i></p> | <p>√</p> <p>√</p> <p>√</p> <p>√</p> <p>X</p>    |
| RAAMbo  | <p>Representative participant population?</p> <p><i>Numbers probably too small esp for males (n=13 overall)</i></p> <p>Allocation (randomisation and allocation concealment adequate)?</p> <p><i>Not enough detail</i></p> <p>Accounted (are all participants accounted for in groups and outcomes)?</p> <p><i>ITT- baseline carried forward stated</i></p> <p>Measurement – blind and/or objective?</p>  | <p>X</p> <p>Unclear</p> <p>√</p> <p>Unclear</p> |

|                              |  |   |
|------------------------------|--|---|
| Intention-to treat analysis? | Was analysis performed in accordance with the principle of intention-to-treat?<br><i>ITT- baseline carried forward stated. Table 2 includes only 37 but this is because of 2 equipment failures.</i>         | √ |
| Confounding                  | Was there any adjustment for potential confounding?<br><i>Randomisation procedure designed to ensure groups were equal in regards to baseline TST and napping. No mention of age, sex, insomnia severity</i> | X |

|                                      |                    |
|--------------------------------------|--------------------|
| <b>Overall assessment of quality</b> | <b>Low quality</b> |
|--------------------------------------|--------------------|

**Risk of Bias (www.cochrane-handbook.org)**

| <b>Domain</b>                          | <b>Judgement</b><br><i>Low risk, high risk, unclear risk</i> | <b>Support for judgement</b>   |
|--|--|--|
| Adequate random sequence generation?   | Unclear risk   | <i>“subjects were assigned to treatment using a randomisation procedure that employed a modification of the Efron procedure”</i>   |
| Allocation concealment?                | Unclear risk   |  |
| Blinding? (participants and personnel) | Unclear risk   | <i>“at no point was the assignment unblinded”. This comment presumably refers to the participants.<br/>“not possible to blind the therapist to a subject’s treatment assignment”<br/>Not clear if the therapist knew the study hypothesis.</i> |
| Blinding of outcome assessment?        | Unclear risk   |  |
| Incomplete outcome data?               | Low risk   | <i>“Hence, 35 subjects completed all phases of the study through follow up”</i>  |

|   |              |   |
|---|--------------|---|
|   |              | <i>Low attrition rate. All available data included in results tables.2 and 3.</i> |
| Selective reporting?                      | Unclear risk |   |
| Other bias?                               | Unclear risk |   |
| <b>Overall assessment of risk of bias</b> |              | <b>Unclear risk</b>   |



|                              |   |
|------------------------------|---|
| <b>Paper:</b> Lichstein 2001 | Relaxation and Sleep Compression for Late-Life Insomnia: A Placebo-Controlled Trial |
|------------------------------|---|

| <b>Variable</b>            | <b>Questions to consider</b>  | <b>Adequate?</b><br>X/√/unclear                                |
|----------------------------|---|--|
| <b>Methods and setting</b> | <p><b>Study design</b><br/>Randomised controlled trial</p> <p><b>Total study duration</b><br/>1 year (6 weeks treatment then post-treatment assessment, follow up at 1year).</p> <p><b>Sequence generation</b> Not mentioned</p> <p><b>Allocation sequence concealment</b> Not mentioned</p> <p><b>Blinding</b> Not mentioned</p> <p><b>Other concerns about bias</b></p> | <p>√</p> <p>√</p> <p>unclear</p> <p>unclear</p> <p>unclear</p> |
| <b>Participants</b>        | <p><b>Total number</b> 89</p> <p><b>Setting</b> Community volunteers</p> <p><b>Diagnostic criteria</b> ICSD</p> <p>Structured interview to rule out medical, psych, substance</p> <p><b>Age</b> Older adults mean age68 (range 59-92)</p> <p><b>Sex</b> Female&gt;male</p> <p><b>Country</b> USA</p> <p><b>Co-morbidity</b> nil</p>                                       | <p>√</p>   |

|                         |   |                   |
|-------------------------|---|-------------------|
|                         | <p><b>Socio-demographics</b> Mainly educated</p> <p><b>Ethnicity</b> Mainly white</p> <p><b>Date of study</b> Not mentioned</p>   |                   |
| <b>Intervention</b>     | <p><b>Total number of intervention groups:</b> 3</p> <p><b>INTERVENTION</b> Sleep Compression<br/> <i>Average TST and time in bed was determined by sleep diaries. The difference was divided by 5, and allotted time in bed compressed by this amount weekly.</i><br/> <i>Nb if napping was included (due to participant resistance), naps ,30 and no later than 2pm were allowed.</i><br/> <i>Revised sleep schedule given each week (sessions 1-5). TIB increased if SE &gt;90%</i></p> <p><b>INTERVENTION</b> Relaxation<br/> <i>10 min hybrid relaxation technique-details given</i></p> <p><b>COMPARISON</b> Placebo desensitisation<br/> <i>Constructing a temporal hierarchy of 10 bedtime events e.g. having a snack, brushing teeth</i></p> | <p>√</p> <p>√</p> |
| <b>Outcome and time</b> | <p>Outcomes and time points</p> <ol style="list-style-type: none"> <li>1. Collected<br/> <i>Post treatment (presumably 6 weeks)</i><br/> <i>Follow up (1 year)</i></li> <li>2. Reported<br/> <i>Post treatment</i></li> </ol>   | <p>√</p>          |

|                |  |                         |
|----------------|--|-------------------------|
|                | <p><i>Follow up (1 year)</i></p> <p><u>Outcome definition</u></p> <p><i>SOL (mins)</i></p> <p><i>NWAK (#)</i></p> <p><i>WASO (mins)</i></p> <p><i>TST (mins)</i></p> <p><i>SE (TST/TIB x 100)</i></p> <p><i>Napping (mins/day)</i></p> <p><i>Sleep stages (PSG)</i></p> <p><i>Sleep quality – 1-5 rating scale 1=very poor, 5=excellent</i></p> <p><i>IIS (Insomnia Impact Scale)</i></p> <p><i>BASS (Beliefs and Attitudes about Sleep Scale)</i></p> <p><i>FSS (Fatigue Severity Scale)</i></p> <p><i>ESS (Epworth Sleepiness Scale)</i></p> |                         |
| <b>Results</b> | <p><b>Number of participants allocated to each intervention group</b></p> <p>Sleep Compression: <i>31 but 24 at follow up (? Only those at f/u analysed)</i></p> <p>Relaxation: <i>30 but 27 at follow up</i></p> <p>Placebo Desensitisation: <i>28 but 23 at follow up</i></p> <p>For each outcome of interest:</p> <p>Sample size: at follow up SC = 24, placebo = 23 <i>not ITT</i></p> <p>Missing participants <i>Yes</i></p>  | <p>Unclear</p> <p>X</p> |

|                              |  |                              |
|------------------------------|--|------------------------------|
|                              | Estimate of effect with confidence interval; P value   | X                            |
| RAAMbo                       | Representative participant population?<br>Allocation (randomisation and allocation concealment adequate)?<br>Accounted (are all participants accounted for in groups and outcomes)?<br>Measurement – blind and/or objective? | √<br>Unclear<br>X<br>Unclear |
| Intention-to treat analysis? | Was analysis performed in accordance with the principle of intention-to-treat?   | X                            |
| Confounding                  | Was there any adjustment for potential confounding? Stratified on gender, SE and Insomnia Impact Scores then randomised within strata.   | Unclear                      |

|                                      |                    |
|--------------------------------------|--------------------|
| <b>Overall assessment of quality</b> | <b>Low quality</b> |
|--------------------------------------|--------------------|

**Risk of Bias (www.cochrane-handbook.org)**

| <b>Domain</b>                          | <b>Judgement</b><br><i>Low risk, high risk, unclear risk</i> | <b>Support for judgement</b>                           |
|--|--|--|
| Adequate random sequence generation?   | Unclear risk   | <i>No mention of random sequence generation method</i> |
| Allocation concealment?                | Unclear risk   | <i>No mention of allocation concealment</i>            |
| Blinding? (participants and personnel) | Unclear risk   | <i>No mention of blinding</i>                          |
| Blinding of outcome                    | Unclear risk   | <i>No mention of blinding</i>                          |

|                          |           |  |
|--------------------------|-----------|--|
| assessment?              |           |  |
| Incomplete outcome data? | High risk | <i>89 randomised but only 74 completers analysed</i> |
| Selective reporting?     | Low risk  |  |
| Other bias?              |           |  |

|   |                     |
|---|---------------------|
| <b>Overall assessment of risk of bias</b> | <b>Unclear risk</b> |
|---|---------------------|

|                              |  |
|------------------------------|--|
| <b>Paper: Fernando, 2013</b> | A double-blind randomised controlled study of a brief intervention of bedtime restriction for adult patients with primary insomnia |
|------------------------------|--|

| <b>Variable</b>     | <b>Questions to consider</b>  | <b>Adequate?<br/>X/√/unclear</b>          |
|---------------------|---|---|
| Methods and setting | <p>Study design: <i>RCT</i></p> <p>Total study duration: <i>6 weeks</i></p> <p>Sequence generation: <i>excel spreadsheet prior to recruitment (is this random number generation?)</i></p> <p>Allocation sequence concealment: <i>One of the investigators generated the sequence, then placed in opaque envelopes. Could possibly foresee sequence allocation therefore possible selection bias.</i></p> <p>Other concerns about bias</p> | <p>√</p> <p>X</p> <p>Unclear</p> <p>X</p> |
| Participants        | <p>Total number: <i>45</i></p> <p>Setting: <i>Community</i></p> <p>Diagnostic criteria: <i>DSM-IV-TR</i></p> <p>Age: <i>≥16</i></p> <p>Sex: <i>male and female</i></p> <p>Country: <i>NZ</i></p> <p>Co-morbidity: <i>no</i></p> <p>Ethnicity: <i>mainly European</i></p> <p>Date of study: <i>March 2006-Jan 2008</i></p>   | √   |
| Intervention        | Total number of intervention groups: <i>2</i>   |   |

|                         |   |                   |
|-------------------------|---|-------------------|
|                         | <p><b>INTERVENTION</b></p> <p><i>Sleep restriction plus sleep hygiene</i></p> <p><i>Personal instructions based on sleep diary info.</i></p> <p><i>Instructions to be adhered to for 6 weeks.</i></p> <p><i>Assume that method is the same as in introduction: limit time in bed to their calculated average sleep time.</i></p> <p><b>COMPARISON</b></p> <p><i>Sleep hygiene alone</i></p> <p><i>No information given as to what instructions were given.</i></p>          | <p>√</p> <p>√</p> |
| <p>Outcome and time</p> | <p>Outcomes and time points</p> <ol style="list-style-type: none"> <li>1. Collected</li> <li>2. Reported</li> </ol> <p><i>6 weeks only (different sleep quality scale used at baseline)</i></p> <p><i>Self reported sleep improvement: Better, much better, same, worse, much worse</i></p>   | <p>X</p>          |
| <p>Results</p>          | <p>Number of participants allocated to each intervention group</p> <p><i>SRT + sleep hygiene n = 22, Control (sleep hygiene) n = 23</i></p> <p>For each outcome of interest:</p> <p>Sample size: <i>as above</i></p> <p>Missing participants: <i>1 in each group (4% attrition)</i></p> <p>Summary data for each intervention group</p> <p><i>Absolute risk of benefit 38% (95% CI 8.8-59%)</i></p> <p><i>NNT = 3 (95% CI 2-11)</i></p> <p><i>Chi squared, p = 0.01</i></p> | <p>√</p>          |

|                              |  | <i>Better or much better</i> | <i>Same, worse, or much worse</i> | <i>Total</i> |                              |
|------------------------------|--|------------------------------|-----------------------------------|--------------|------------------------------|
|                              | <i>Intervention</i>  | 16                           | 6                                 | 22           |                              |
|                              | <i>Control</i>   | 8                            | 15                                | 23           |                              |
| RAAMbo                       | Representative participant population?<br>Allocation (randomisation and allocation concealment adequate)?<br>Accounted (are all participants accounted for in groups and outcomes)?<br>Measurement – blind and/or objective? |                              |                                   |              | Unclear<br>Unclear<br>✓<br>✓ |
| Intention-to treat analysis? | Was analysis performed in accordance with the principle of intention-to-treat?   |                              |                                   |              | ✓                            |
| Confounding                  | Was there any adjustment for potential confounding?  |                              |                                   |              | X                            |

|                                      |   |
|--------------------------------------|---|
| <b>Overall assessment of quality</b> | Reasonable quality but very short term and outcome measure not validated. |
|--------------------------------------|---|

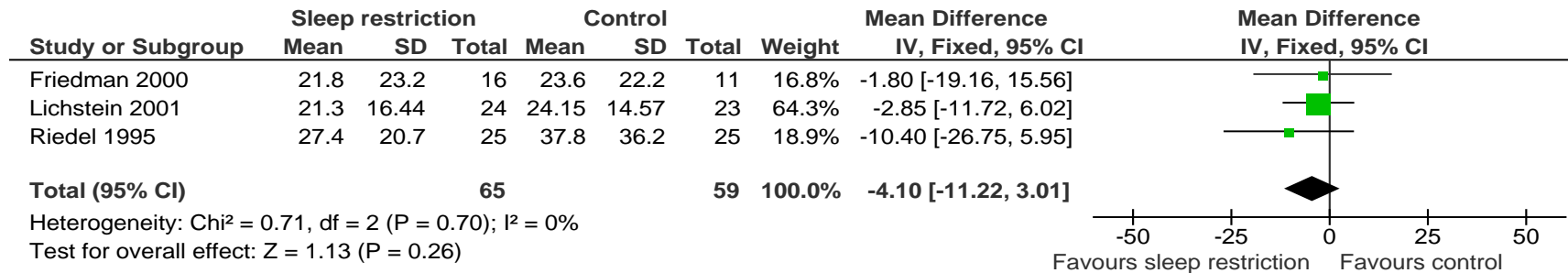
**Risk of Bias (www.cochrane-handbook.org)**

| <b>Domain</b>                        | <b>Judgement</b><br><i>Low risk, high risk, unclear risk</i> | <b>Support for judgement</b>   |
|--------------------------------------|--|--|
| Adequate random sequence generation? | Low risk   | <i>“Randomisation was done by one of the investigators using a Microsoft Office Excel spreadsheet”</i> |

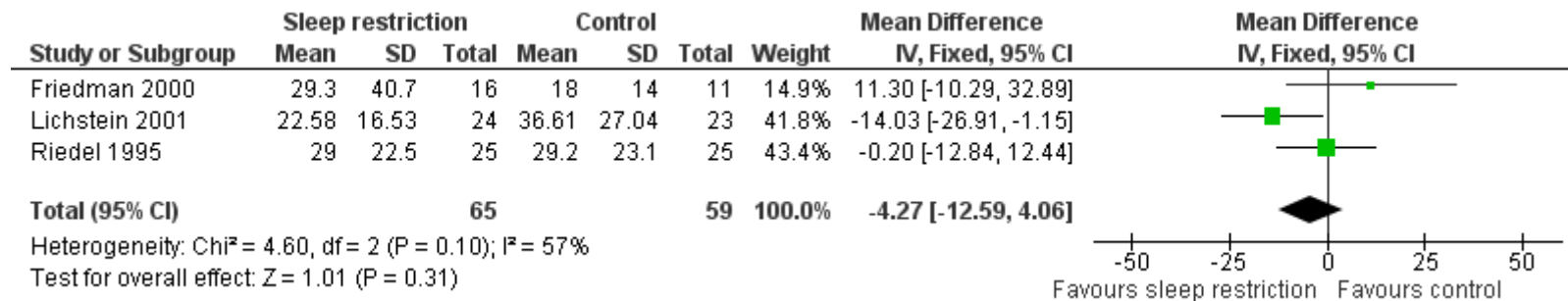


|   |              |  |
|---|--------------|--|
|   |              | <i>Is this random number generation? If so, low risk</i>   |
| Allocation concealment?                   | Unclear risk | <i>One of the investigators generated the sequence. However, allocations were then placed in sealed numbered opaque envelopes which were then opened in order. This suggests the investigator may have had prior knowledge of the sequence which could lead to selection bias.</i>   |
| Blinding? (participants and personnel)    | Low risk     | <i>“Care was taken not to disclose which group each participant was in”<br/>Participants were blinded.<br/>The investigators were not blind to the allocation.<br/>“The staff member was instructed not to ask about the patient’s intervention and so remained blind to the intervention”.<br/>Outcomes assessor was blinded.</i> |
| Blinding of outcome assessment?           | Low risk     | <i>“The staff member was instructed not to ask about the patient’s intervention and so remained blind to the intervention”.<br/>Outcomes assessor was blinded.</i>   |
| Incomplete outcome data?                  | Low risk     | <i>Text states: “those who were lost to follow up were allocated their baseline status”<br/>Table 2 states “Assumes those lost to follow-up were sleeping ‘worse’ ”.<br/>Only 2 lost to follow up (one from each group), so low attrition rate.</i>  |
| Selective reporting?                      | Unclear      | <i>No protocol registered as before trials registry started.</i>   |
| Other bias?                               |              |  |
| <b>Overall assessment of risk of bias</b> |              | Low risk   |

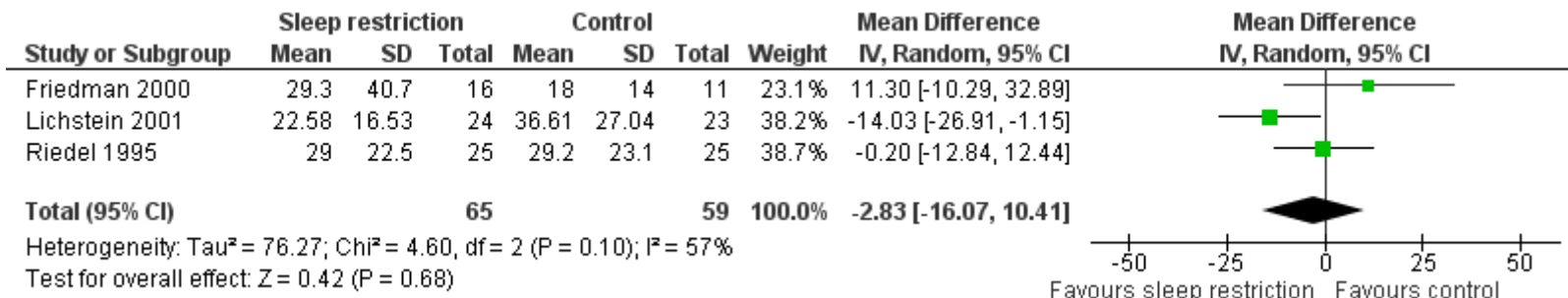
## Appendix E: Systematic Review of Sleep Restriction for Primary Insomnia: Meta-Analysis Forest Plots



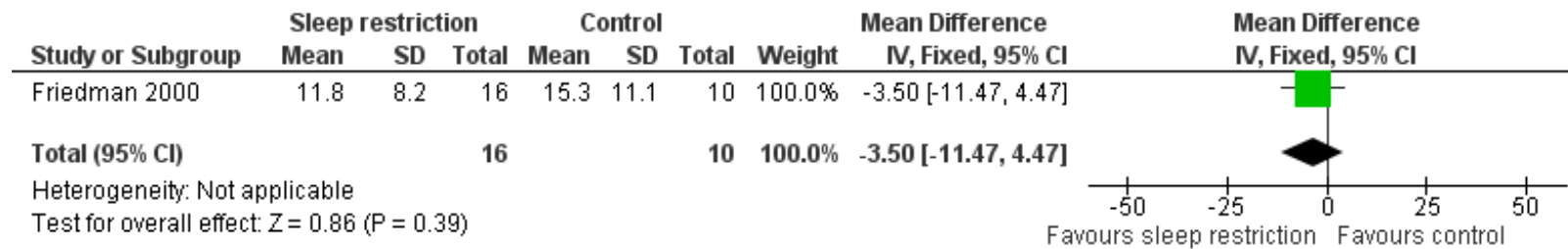
i. Meta-analysis comparing sleep diary sleep-onset latency at post-treatment for sleep restriction versus control groups



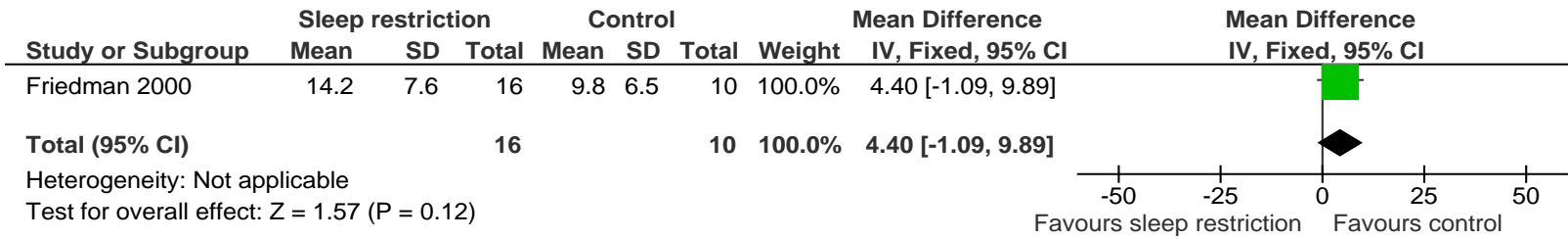
ii. Meta-analysis comparing sleep diary sleep-onset latency at follow up for sleep restriction versus control groups – fixed effects model



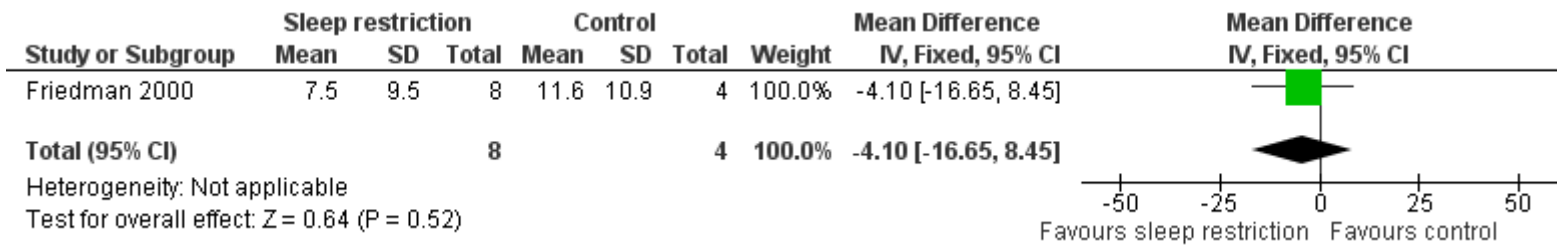
iii. Meta-analysis comparing sleep diary sleep-onset latency at follow up for sleep restriction versus control groups – random effects model



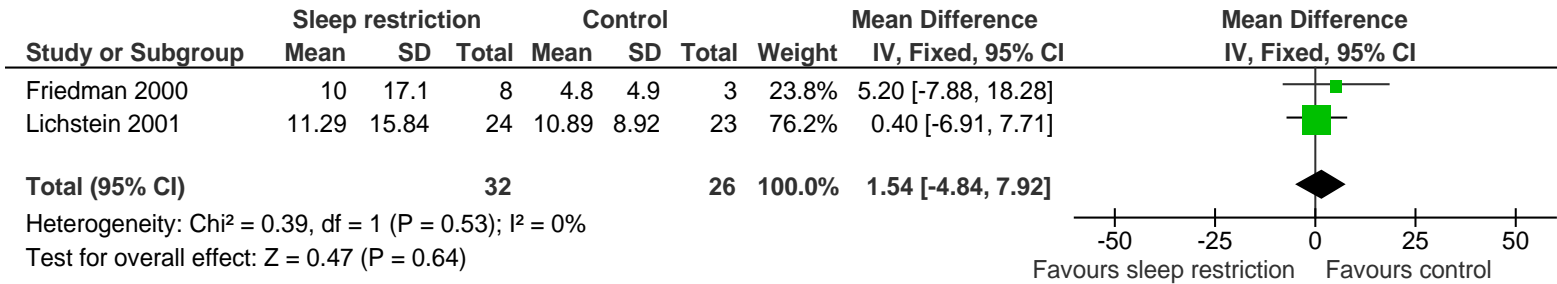
iv. Sleep-onset latency measured by actigraphy at post-treatment for sleep restriction versus control group



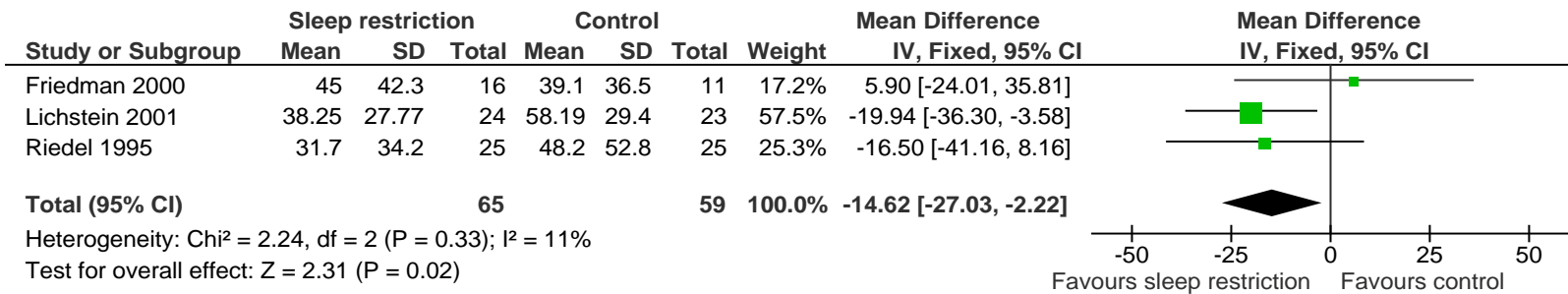
v. Sleep-onset latency measured by actigraphy at follow up for sleep restriction versus control group



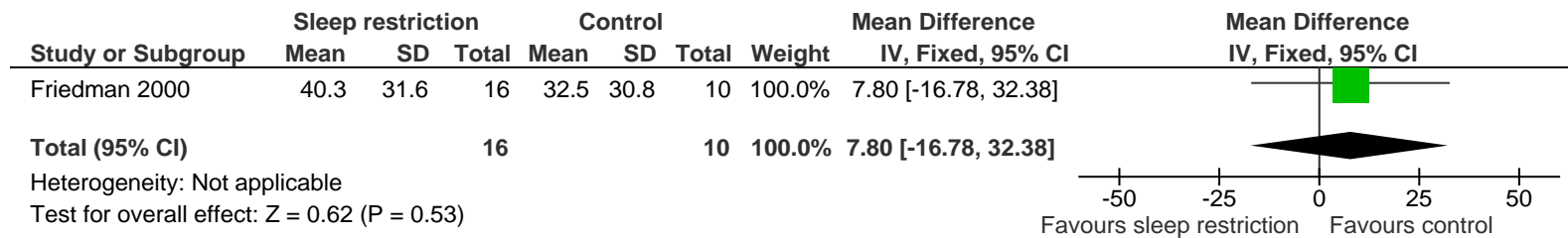
vi. Sleep-onset latency measured by polysomnography at post-treatment for sleep restriction versus control group



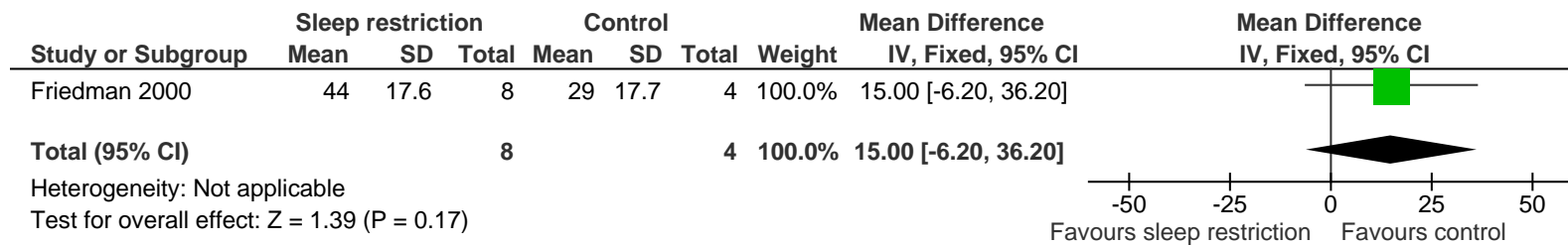
vii. Sleep-onset latency measured by polysomnography at follow up for sleep restriction versus control group



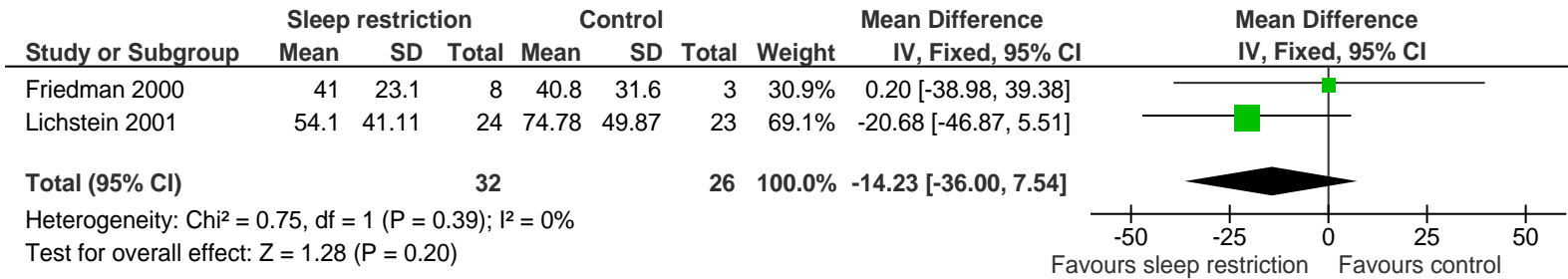
viii. Meta-analysis comparing sleep diary wake after sleep onset at follow up for sleep restriction versus control groups



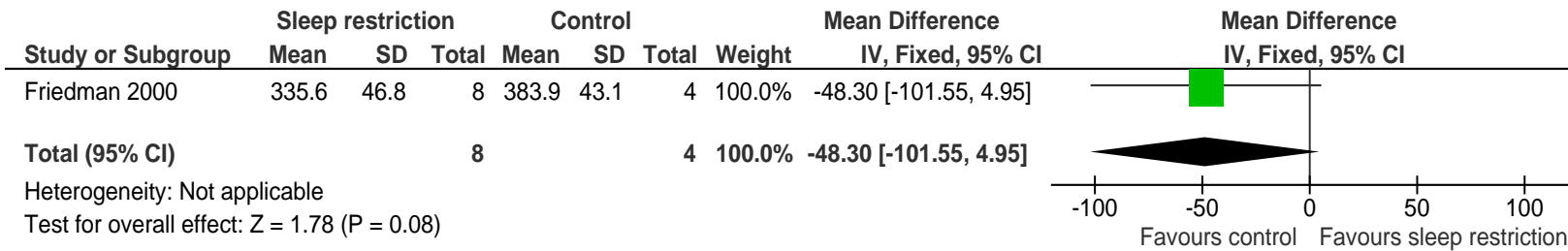
ix. Wake after sleep onset measured by actigraphy at follow up for sleep restriction versus control group



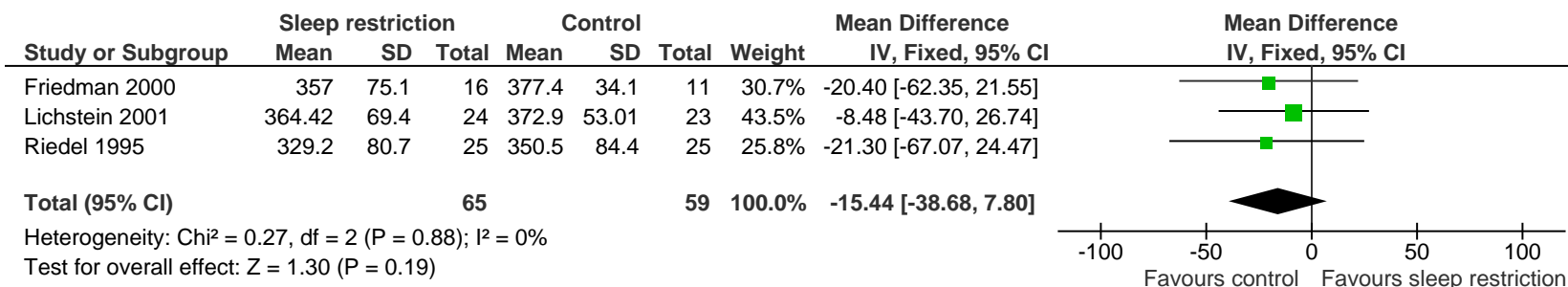
x. Wake after sleep onset measured by polysomnography at post-treatment for sleep restriction versus control group



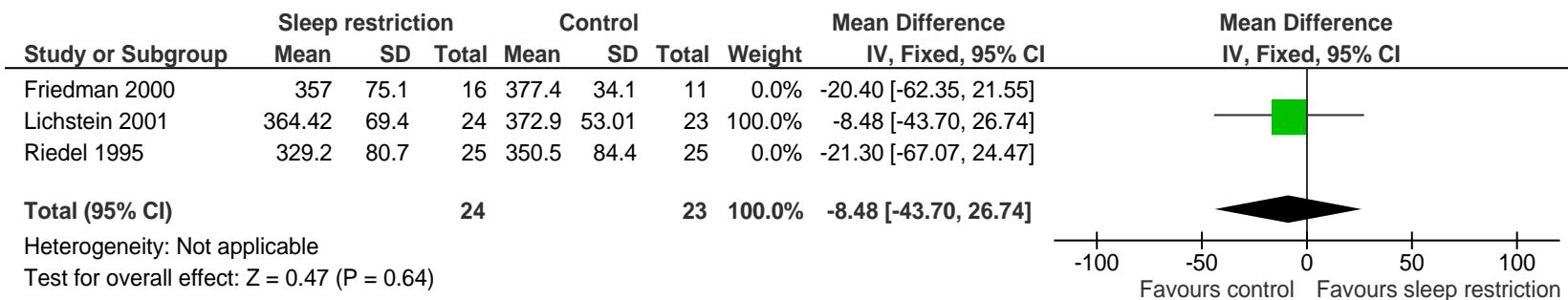
xi. Meta-analysis comparing wake after sleep onset measured by polysomnography at follow up for sleep restriction versus control group



xii. Total sleep time measured by polysomnography at post-treatment for sleep restriction versus control group

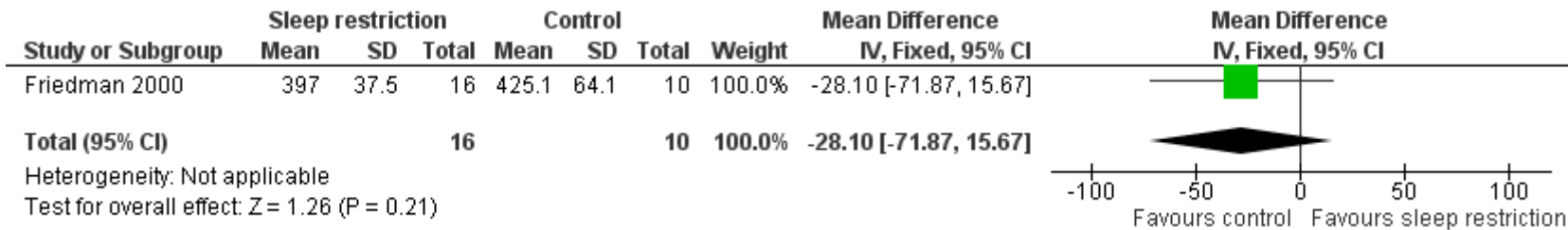


xiii. Meta-analysis comparing total sleep time measured by sleep diary at follow up for sleep restriction versus control groups

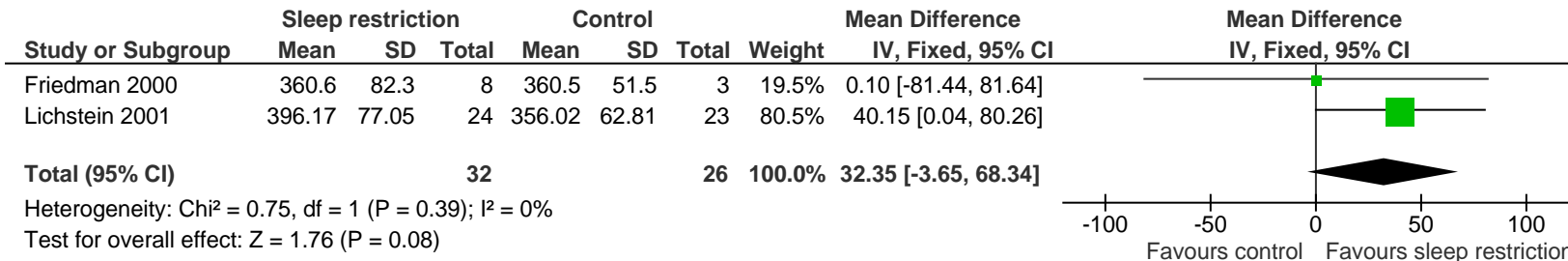


xiv. Total sleep time measured by sleep diary at one year follow up for sleep restriction versus control groups

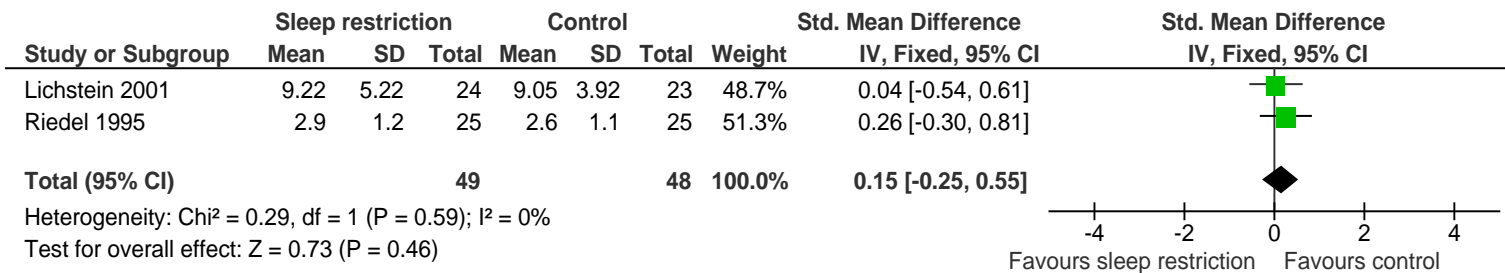




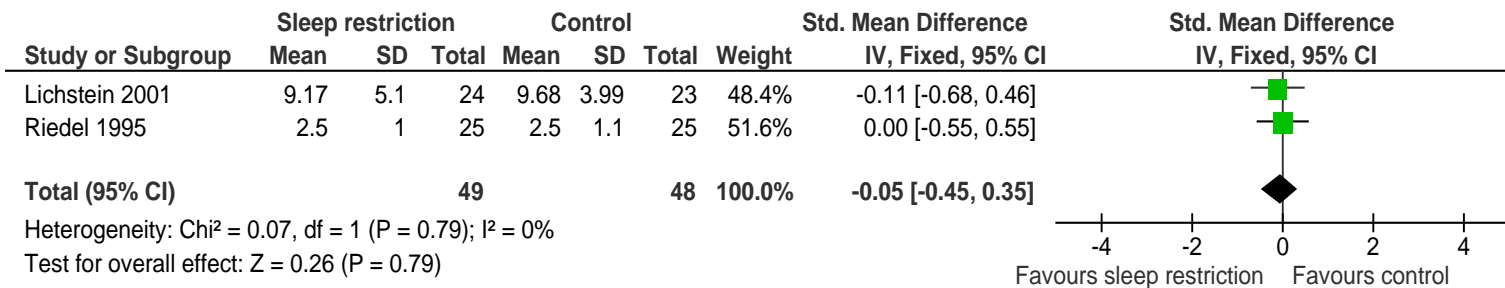
xv. Total sleep time measured by actigraphy at follow up for sleep restriction versus control group



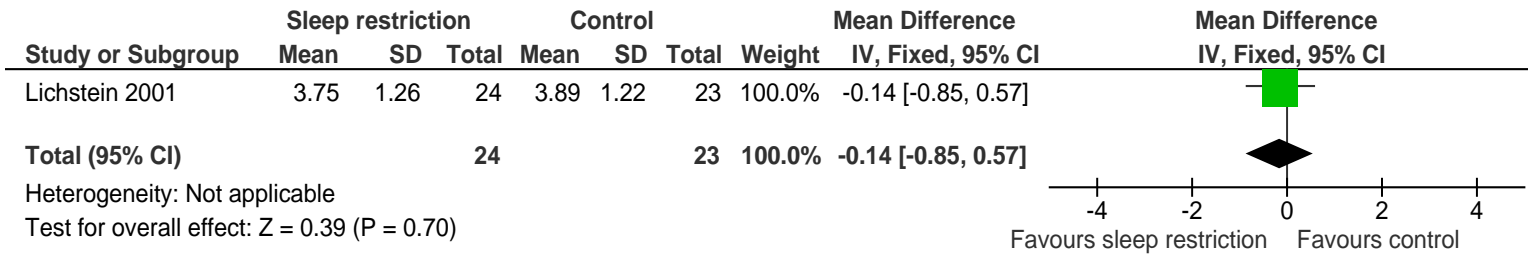
xvi. Meta-analysis comparing total sleep time measured by polysomnography at follow up for sleep restriction versus control groups



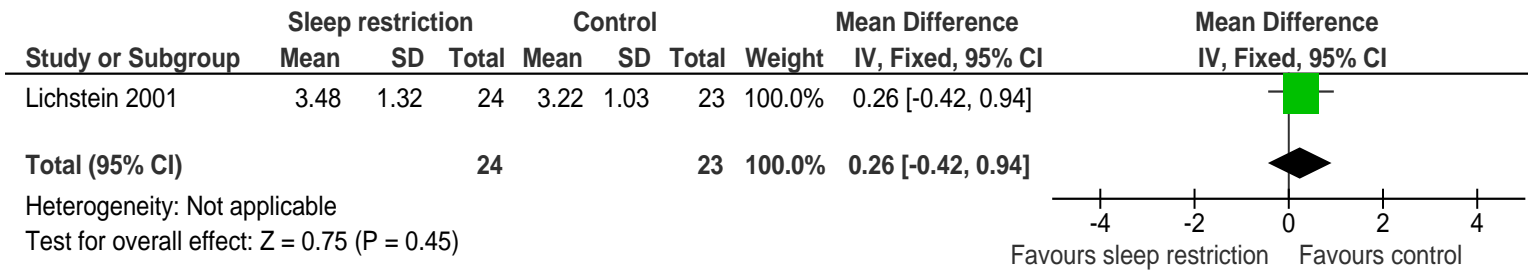
xvii. Meta-analysis comparing sleepiness at post-treatment for sleep restriction versus control groups



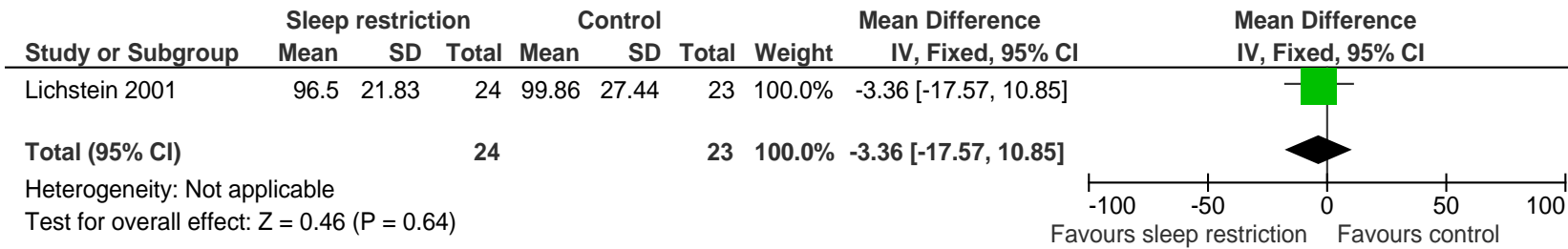
xviii. Meta-analysis comparing sleepiness at follow up for sleep restriction versus control groups



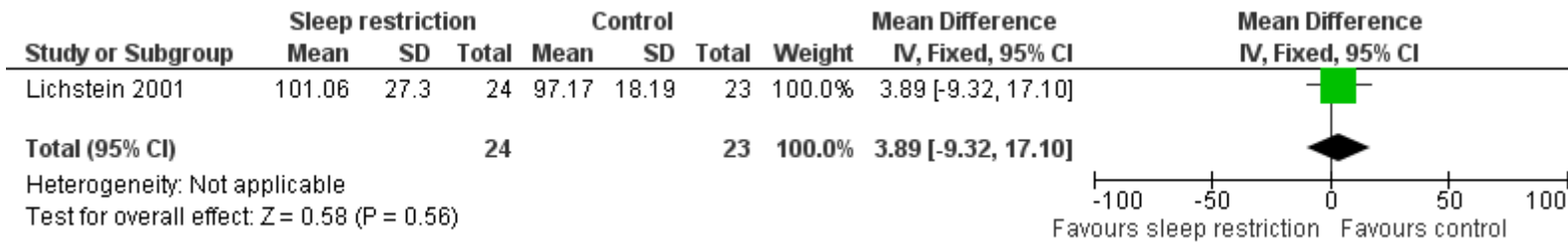
xix. Fatigue at post-treatment for sleep restriction versus control group



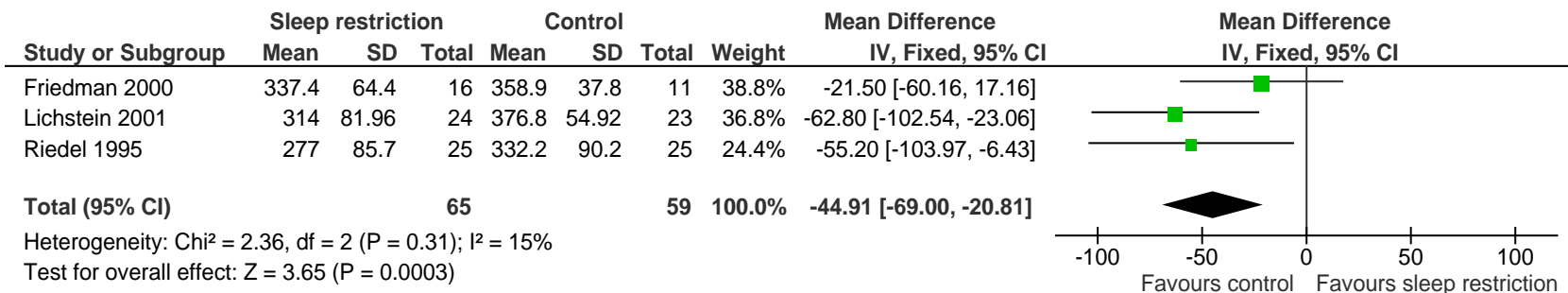
xx. Fatigue at follow up for sleep restriction versus control group



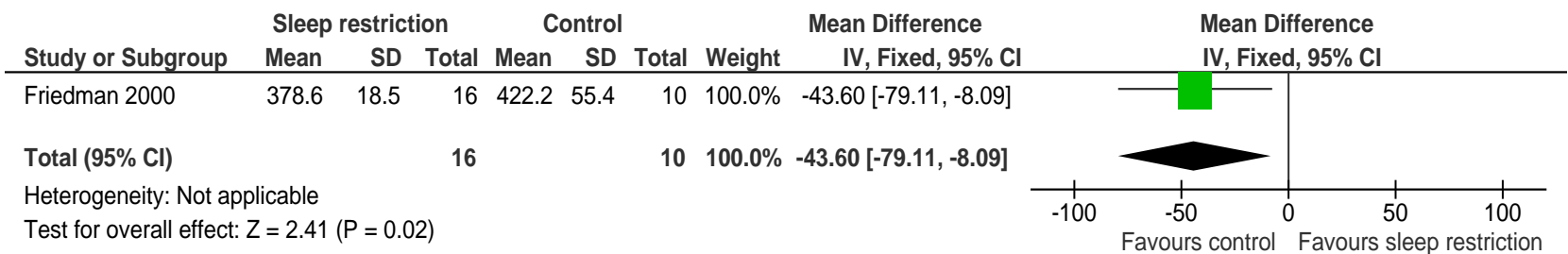
xxi. Insomnia Impact Scale score at post-treatment for sleep restriction versus control



xxii. Insomnia Impact Scale score at follow up for sleep restriction versus control



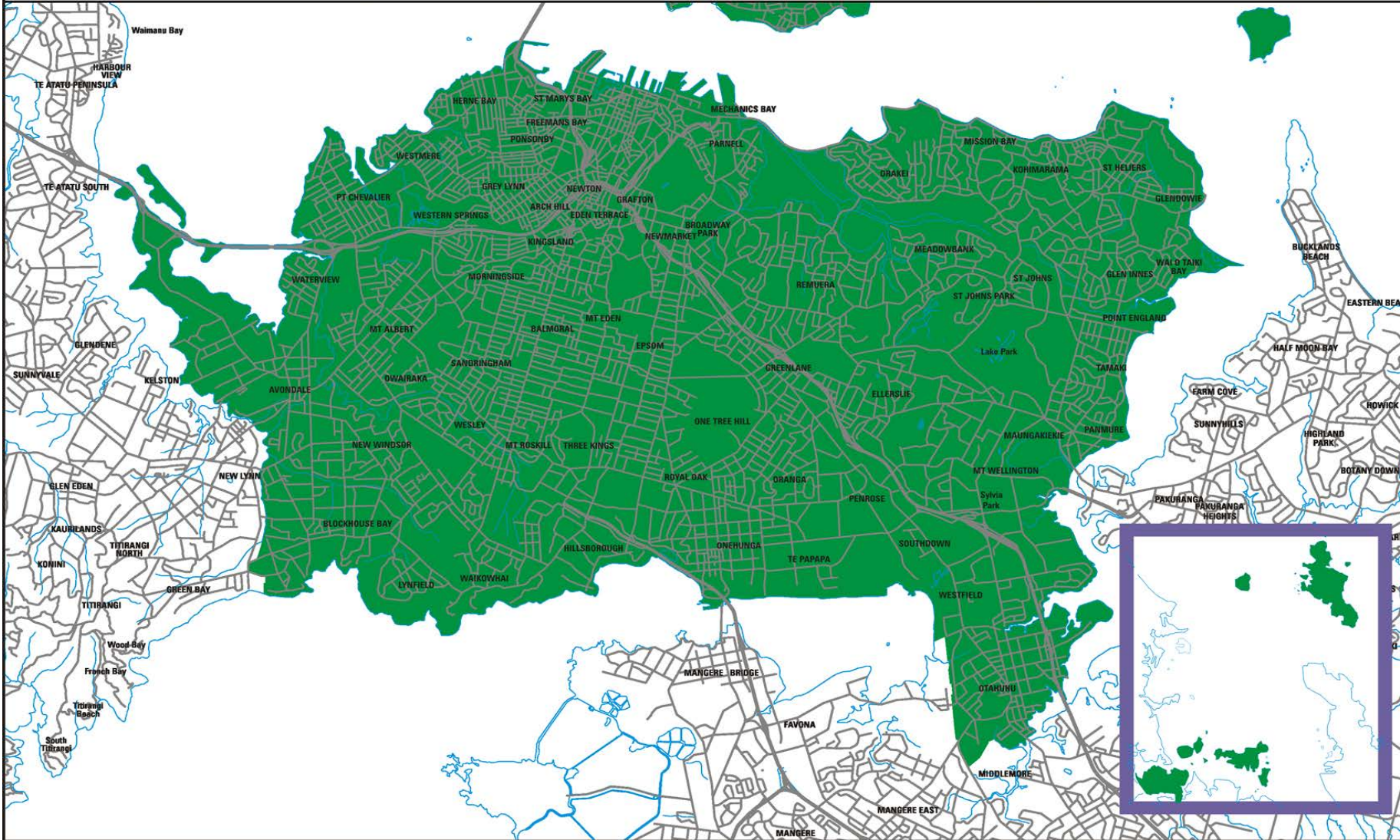
**xxiii. Meta-analysis comparing total sleep time measured by sleep diary at post-treatment for sleep restriction versus control groups**



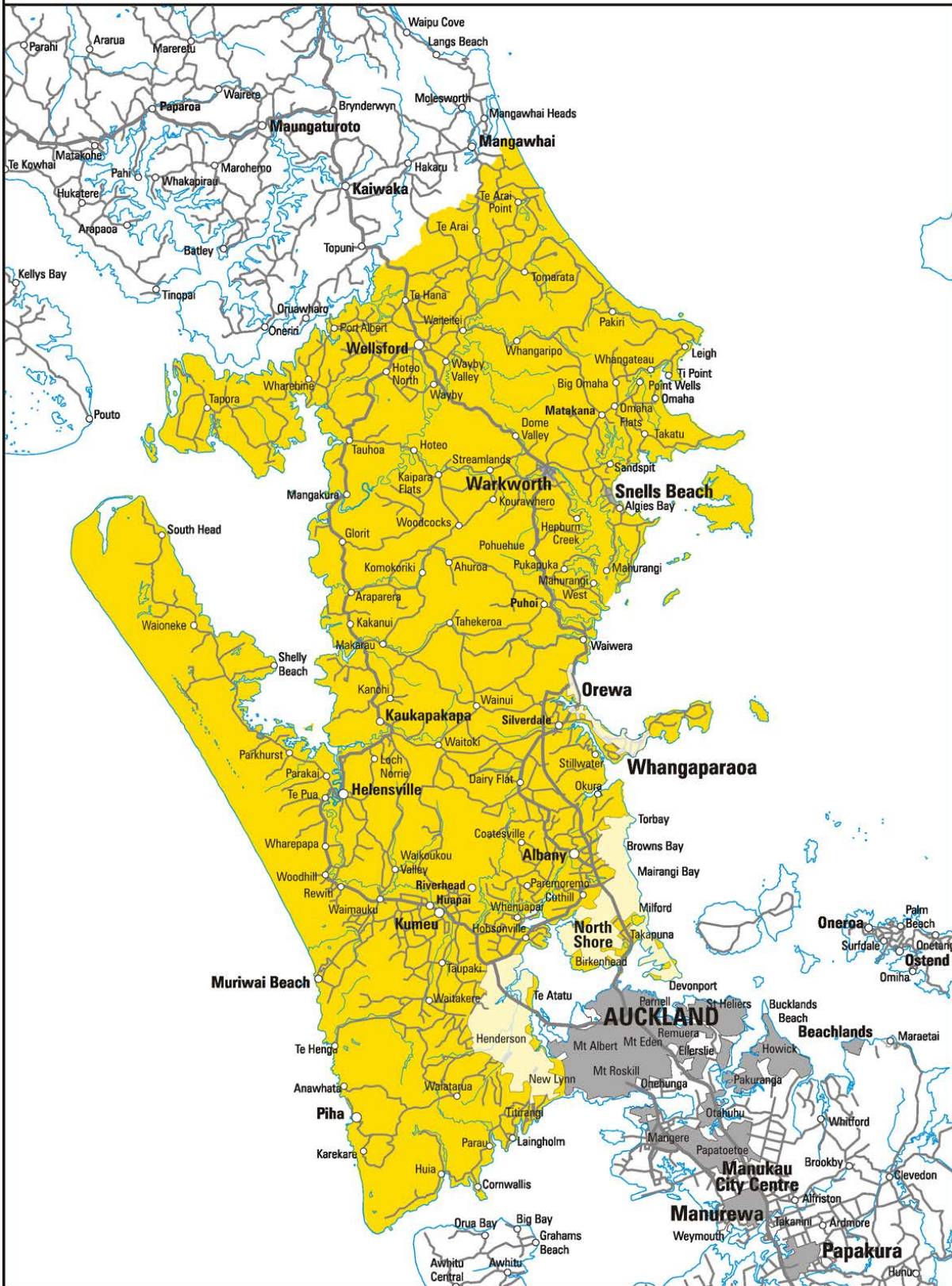
**xxiv. Total sleep time measured by actigraphy at post-treatment for sleep restriction versus control group**

# Appendix F: Auckland and Waitemata District Health Board Catchment Areas

## AUCKLAND DISTRICT HEALTH BOARD (Hauraki Gulf Islands included in Auckland DHB)



# WAITEMATA DISTRICT HEALTH BOARD



Reproduced with permission from the Ministry of Health. <http://www.health.govt.nz/new-zealand-health-system/key-health-sector-organisations-and-people/district-health-boards/location-boundaries-map>

## Appendix G: Study Invitation Letter (Q1)

### Practice Letterhead

Professor Bruce Arroll (Head of the Department of General Practice), Dr Antonio Fernando (Psychiatrist and Insomnia Specialist) and their team at The University of Auckland are conducting a study regarding sleep. They would like to recruit participants into a research study looking at non-drug treatments for insomnia (poor sleep). This research will also contribute to a doctoral thesis (PhD).

- Our practice is supporting this research by sending letters introducing this study to our patients – you have been contacted as you are aged between 16 and 75 years old
- If you have problems sleeping sending this completed questionnaire to the researchers at the university may mean they would be interested in asking you to participate further in the study

Kind regards,

Dr

⇒ Please complete the questions below **if you have poor sleep** and are interested in participating in the study.

1. During the past month, how would you rate your sleep quality overall? (Please tick one box)

Very good  Fairly good  Fairly bad  Very bad

2. a. Do you have trouble with your sleeping (i.e. difficulty initiating sleep, difficulty maintaining sleep, waking up too early, or sleep that is nonrestorative or poor in quality) such that it interferes with your function the following day? (see examples in box)

Yes  No

b. Does this occur 3 or more times per week?

Yes  No  Not applicable

Ways that poor sleep can affect function

- Fatigue or malaise
- Attention, concentration or memory impairment
- Social or vocational dysfunction or poor school performance
- Mood disturbance or irritability
- Daytime sleepiness
- Motivation, energy or initiative reduction
- Proneness for errors or accidents at work or whilst driving
- Tension, headaches, or gastrointestinal symptoms in response to sleep loss
- Concerns or worries about sleep

c. Does your difficulty sleeping occur even when you give yourself adequate opportunity to sleep (that is, allowing yourself enough time to have a good sleep and not “burning the candle at both ends”)?

Yes, I still sleep poorly even when I have enough time to sleep

No  Not applicable

3. How WORRIED/distressed are you about your current sleep problem? (please circle one response)

Not at all worried/  
not applicable                      A little                      Somewhat                      Much                      Very much  
0    1    2    3    4  
worried

⇒ Please fill in your contact details if you have poor sleep and would like to be contacted by the University researchers about the insomnia study.

Name:

Postal address:

Phone number:

Send the questionnaire to the University researchers by post in the Freepost envelope provided, or by fax to (09)373 7624, or by scanning and email to [sleepstudy@auckland.ac.nz](mailto:sleepstudy@auckland.ac.nz)



## Appendix H: Comprehensive Questionnaire (Q2)



# THE UNIVERSITY OF AUCKLAND

## FACULTY OF MEDICAL AND HEALTH SCIENCES

### School of Population Health Insomnia Treatment Study

Name:.....

(Please tick appropriate boxes below)

(a) **Gender:**             Male             Female

(b) **Age** (in years):        ..... Date of birth: ...DD/MM/YY.

(c) **To which ethnic group(s) do you belong?**

NZ European/Pakeha

Maori: Iwi .....

Pacific nations .....(please specify)

Asian..... (please specify)

Other.....(please specify)

(d) **Occupation:**

Employed fulltime

Employed part-time

Student

Retired

Homemaker

Unemployed

Sickness benefit

This questionnaire only takes approximately 5 minutes

**Please complete and return within 2 weeks**

All completed responses go in the draw to win \$200 worth of Westfield vouchers

You may be contacted based on your answers to this questionnaire if you fit the criteria to participate in our trial of a non-drug treatment for insomnia.

#### Contact details:

Home phone number:..... Work number:.....

Mobile number:..... Email:.....

What is (are) the best time(s) to contact you? .....

Please consider whether or not you consent to your questionnaire responses being forwarded to your GP for inclusion into your medical records.

This information may assist your GP in your provision of healthcare.

However, it is important to remember that in certain situations (e.g. applying for life or health insurance) insurance companies may ask permission to have access to the medical records held by your GP/family doctor. Some of the information we have requested may have implications for this. On the other hand, your GP may already be aware of a lot of your answers.



I would like the information from the questionnaire to go into my medical records

YES / NO (please circle)

My GP is: \_\_\_\_\_

**Q1 Your answers to the previous questionnaire indicate you have a problem with sleeping:**

How WORRIED/distressed are you about your current sleep problem? (please circle one response)

|                    |          |          |      |                   |
|--------------------|----------|----------|------|-------------------|
| Not at all worried | A little | Somewhat | Much | Very much worried |
| 0                  | 1        | 2        | 3    | 4                 |

a. How long has this been a problem? .....

b. Was there some event that caused this? (please describe below)

.....

**c. During the past month, how often have you had trouble sleeping because you...**

*(please check the one best response)*

i. Cannot get to sleep within 30 minutes:

- Not during the past month
- Less than once a week
- Once or twice a week
- Three or more times a week

Office use only:  
PSQI 5a

ii. Wake up in the middle of the night or early morning:

- Not during the past month
- Less than once a week
- Once or twice a week
- Three or more times a week

Office use only:  
PSQI 5b

**d. During the past month, how would you rate your sleep quality overall?**

- Very good
- Fairly good
- Fairly bad
- Very bad

Office use only:  
PSQI 6

**e. Have you discussed your problems with sleep with a doctor?**  Yes  No

- If **No**, what is the reason for this? :
- The sleep problem started since last visit to GP
  - Did not think it was important enough
  - Did not think anything could be done for it
  - Concerned I may be given medication for it
  - Other: *(please describe)*:

**Q2**

**a. Do you find your bed/bedroom uncomfortable or annoying?**  No  Yes

If **Yes**, why is this? .....

**b. Are you bothered by loud noise or lights that distract you from sleeping?**

- No  Yes

If **Yes**, please explain: .....

**c. Do you have a regular bed partner who shares your bed with you whilst you are asleep?**

- No  Yes

If **Yes**, do you feel your sleep is disrupted by your bed partner?  No  Yes

If **Yes**, please explain: .....

**d. Do you routinely use alcohol, nicotine (cigarettes) or caffeine (coffee, cola, tea, chocolate) in the evenings?**

- No  Yes

- e. Do you engage in mentally stimulating, moderate to strenuous exercise, or emotionally upsetting activities within a couple of hours of bedtime more than three times a week?  
 No                       Yes
  
- f. Do you frequently use the bed for activities other than sleep or intimacy (e.g., television watching, reading, studying, snacking, thinking, planning)  
 No                       Yes
  
- g. Do you frequently nap during the day or have highly irregular and variable bedtimes or rising times?  
 No                       Yes

**Q3**

a. During the past month, how often have you taken medicine (prescribed or “over the counter”) to help you sleep?

- Not during the past month
- Less than once a week
- Once or twice a week
- Three or more times a week

Office use only:  
PSQI 7

b. Are you taking any regular medications – either prescribed by the doctor or from the chemist or from the health shop?

- No                       Yes

If **Yes**, Please list all the medications or herbal/health food shop preparations you are taking regularly (more than 3 times per week):

.....

.....

.....

.....

**IMPORTANT:**  
 Your answers to this questionnaire are confidential. However, the exception to confidentiality will be if the interviewer/researcher has significant concern about the safety of yourself or others. In this case the appropriate person such as your GP will be informed.

Q4 a. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

- No problem at all
- Only a very slight problem
- Somewhat of a problem
- A very big problem

Office use only:  
PSQI 9

**b. Over the last 2 weeks, how often have you been bothered by any of the following problems?**  
(Please circle the number that applies to you including not at all where that is the case)

**PHQ-9 (R. L. Spitzer et al., 1999)**

**NB. If you have had thoughts that you would be better off dead or of harming yourself your GP will automatically be notified – it is advised that you speak to your GP about this**

**Q5**

**Over the last 2 weeks, how often have you been bothered by any of the following problems? (Please circle the number that applies to you including not at all where that is the case)**

**GAD-7 (Kroenke et al., 2007)**

**Q6**

a. **Are you a shift worker?**  No (go to Q7)  Yes

b. **Type of shift** (tick one box):

- i. the same shifts e.g. night shift
- ii. rotating shifts
- i. a combination of the above

c. **Do you have problems with your sleep that you think may be caused by being a shift worker?**  No  Yes

**Q7**

**Women only** (men go to Q9)

**Are you pregnant, breastfeeding or less than 6 months since giving birth?**

- No
- Yes

**Q8**

**Women only** (men go to Q9)

**a. Are you postmenopausal?**  No  Yes

**b. Do you experience hot flushes?**  No (go to Q9)  Yes.

i. How many times per night do you awaken due to hot flushes?

.....

ii. Do these significantly affect your sleep?  No  Yes

iii. How many nights per week do you experience insomnia due to the hot flushes?

- Not during the past month
- Less than once a week
- Once or twice a week
- Three or more times a week

**Q9**

**Regarding the use of alcohol:**

CAGE questionnaire (Ewing, 1984)

**Q10**

**a. Do you have any health problems that significantly affect your ability to sleep well most nights (such as breathing difficulty or acid reflux or night cough or pain or needing to urinate 3 or more times per night)?**

- No
- Yes

Please describe the problem and how many night's sleep per week on average are disrupted because of it:

.....

**b. During the past month, how often have you had trouble sleeping because you:**

i. Have to get up to use the bathroom

- Not during the past month
- Less than once a week
- Once or twice a week
- Three or more times a week

Office use only:  
PSQI 5

ii. Cannot breathe comfortably

- Not during the past month
- Less than once a week
- Once or twice a week
- Three or more times a week

Office use only:  
PSQI 5

iii. Feel too cold

- Not during the past month
- Less than once a week
- Once or twice a week
- Three or more times a week

Office use only:  
PSQI 5

iv. Feel too hot

Not during the past month

Less than once a week

Once or twice a week

Three or more times a week

Office use only:  
PSQI 5

v. Have pain

Not during the past month

Less than once a week

Once or twice a week

Three or more times a week

Office use only:  
PSQI 5

vi. Other reason(s) please describe:

Not during the past month

Less than once a week

Once or twice a week

Three or more times a week

Office use only:  
PSQI 5

**Q11 a. During the past month, how often have you had trouble sleeping because you cough or snore loudly**

Not during the past month

Less than once a week

Once or twice a week

Three or more times a week

Office use only:  
PSQI 5

**b. Do you:**

- i. Snore very loudly -  No  Yes
- ii. Get morning headaches -  No  Yes
- iii. Have a dry mouth upon awakening?  No  Yes

**c. Do you wake with breath holding, gasping or choking?**  No  Yes

**d. Have you ever been told you have loud snoring or “stop breathing” /pause breathing while you are asleep?**  No  Yes → please state which: .....

**a. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?**

Not during the past month

Less than once a week

Once or twice a week

Three or more times a week

Office use only:  
PSQI 8

**b. How likely are you to doze off or fall asleep in the following situations, in contrast to just feeling tired?:**

- would never doze = 0
- slight chance of dozing = 1
- moderate chance of dozing = 2
- high chance of dozing = 3

Office use only:ESS=

| Situation <small>(Epworth Sleepiness Scale copyright © MW Johns 1990-1997)</small> | Chance of dozing (0-3) |
|--|------------------------|
| Sitting and reading  |                        |
| Watching tv  |                        |
| Sitting, inactive in a public place (eg theatre or meeting)                        |                        |
| As a passenger in a car for an hour without a break                                |                        |
| Lying down to rest in the afternoon when circumstances permit                      |                        |
| Sitting and talking with someone   |                        |
| Sitting quietly after a lunch without alcohol                                      |                        |
| In a car, while stopped for a few minutes in the traffic                           |                        |

**Q12**

**a. At night or in the evening, do you get unpleasant sensations in your legs (urge to move, aches, pains, creeping sensations) which affect your sleep?**

- No (go to Q13)                       Yes

If Yes,

- i. Does the urge to move or the unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting?**  
 No     Yes
- ii. Are these sensations partially or totally relieved by movement, rubbing or walking?**  
 No                       Yes
- iii. On average, how frequently do these sensations disturb your sleep?**  
 Less than three nights per week  
 Three or more nights per week

**Q13**

**a. Do you have difficulty falling asleep before 1am and a difficulty awakening at the desired time or at a socially acceptable time (that is, in time for school or work to start)?**

- No                       Yes

**b. In the weekends or on holiday (when you can sleep when you want) do you go to sleep late (after 1am) and wake up in the late morning or afternoon and feel like you have had a good night's sleep?**

- No                       Yes

**c. Do you have difficulty staying awake in the early evening (6-9pm)?**

- No                       Yes

**d. Do you typically wake between 2-5am in the morning?**

- No                       Yes

**e. If you can follow your own sleep schedule (e.g. on holidays or at weekends), do you go to bed before 9pm and wake before 5am and feel like you have had a good night's sleep?**

- No                       Yes

For the below questions your answers should indicate the most accurate reply for the *majority* of days and nights in the past month:

**f. During the past month, when have you usually gone to bed at night?**

.....

USUAL BED TIME

Office use only:  
PSQI 1

**g. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?**

NUMBER OF MINUTES .....

Office use only:  
PSQI 2

**h. During the past month, when have you usually gotten up in the morning?**

UP TIME .....

USUAL GETTING

Office use only:  
PSQI 3

**i. During the past month, how many hours of *actual sleep* did you get at night? (This may be different from the hours you spend in bed) HOURS OF SLEEP PER NIGHT .....**

Office use only:  
PSQI 4

**j. If you have problems with poor sleep, are they related to Jet-Lag or flying across time zones?**

- No  Yes

**Q14**

**a. Do you sleep walk?**  No (go to Q15)  Yes

**b. Did this start before you were a teenager?**  No  Yes

i. When you are walking in your sleep is it difficult for others to wake you up?  
 No  Yes

ii. Do you have trouble remembering the episode(s) of sleep walking?  
 No  Yes

iii. Do these sleep walking episodes occur during the first third of your time asleep?  
 No  Yes

**c. Does your sleep walking affect you or people around you in any way?**

- No  Yes

If **Yes**, in what way? .....

**d. Is your sleep walking severe enough to affect your sleep?**  No  Yes

**e. How often do you sleep walk?**  only occasionally  
 at least weekly  
 three or more times per week  
 not sure

**Q15**

**a. Do you grind your teeth or clench your teeth when asleep?**

- No  Yes

**b. Do you have:**

- i. Abnormal wear of your teeth?  No  Yes  
ii. Sounds associated with teeth grinding?  No  Yes  
iii. Jaw muscle discomfort?  No  Yes

**c. Is your teeth grinding severe enough to affect your sleep?**  Not sure  No  Yes

**Q16**

**a. During the past month, how often have you had trouble sleeping because you have had bad dreams?**

- Not during the past month   
Less than once a week   
Once or twice a week   
Three or more times a week

Office use only:  
PSQI 5

**b. Do you ever have recurrent severe nightmares that wake you up?**

- No  Yes

1. If **Yes**, how often does this happen? Not during the past month   
Less than once a week   
Once or twice a week   
Three or more times a week



**Q17**

**Do you ever wake up in the middle of the night having an anxiety or panic attack? (palpitations, pounding heart, difficulty breathing, shaking, feeling faint?)**

- No                       Yes

- c. If **Yes**, how often does this happen?                      Not during the past month                        
Less than once a week                        
Once or twice a week                        
Three or more times a week

**It is important to remember that in certain situations (e.g. applying for life or health insurance) insurance companies may ask permission to have access to the medical records held by your GP/family doctor. Some of the information we have requested may have implications for this if you have indicated you would like a copy to be sent to your GP.**

**Q18**

- a. **Have you ever taken any non-prescription drugs to get high, to feel better or to change your mood over the past 3 months?**

- No  (*please go to Q19*)                      Yes

2. If **Yes**, how often do you use them?                      Not during the past month                        
Less than once a week                        
Once or twice a week                        
Three or more times a week

- b. **Do you think the use of drugs is affecting your sleep either when you are taking them or after you stop taking them?**                       No                       Yes

- c. **Do you think the use of these drugs affects your quality of sleep?** (while you are using them or after you stop taking them)                       No                       Yes

**Q19 Regarding your medical health:**

- a. Have you suffered from a heart attack in the past 6 months?                       No                       Yes
- b. Have you suffered from a stroke in the last 6 months?                       No                       Yes
- c. Do you suffer from:
- i. Ongoing chest pains/angina?                       No                       Yes
  - ii. Dizziness?                       No                       Yes
  - iii. Fainting attacks/severe lightheadedness?                       No                       Yes
  - iv. Shortness of breath that stops you from walking across the room?                       No                       Yes

**Q20 Regarding your occupation:**

Are you retired?                      Yes                                            *Thank you, the questionnaire is finished*

No                                            Please answer the below questions:

- a. Does your job involve operating a passenger vehicle, truck or heavy vehicle?                       No                       Yes
- b. Does your job involve working with machinery or power tools?                       No                       Yes
- c. If you are more fatigued than usual from a lack of sleep, would this be dangerous for your job? (e.g. if you were a surgeon, construction worker)                       No                       Yes

**Q21 Is there anything else happening in your sleep that we have not covered in the questionnaire? If Yes, please describe:**

*Thank you for taking the time to complete this survey. You may be contacted if you are eligible to participate in our trial of non-drug treatment for insomnia*

Please check you have answered each question

## Appendix I: Participant Information Sheet



### Participant Information Sheet

Effectiveness of a non-drug treatment for primary insomnia

Professor Bruce Arroll (Head of the Department of General Practice), Dr Antonio Fernando (Psychiatrist and Insomnia Specialist) and their team at The University of Auckland are conducting a study regarding sleep. This study is the basis of a doctoral thesis (PhD).

- **You have been invited to take part in this study because the questionnaire from your family doctor or your response to the sleep study flyer indicated that you have a problem with poor sleep.**
- **We would like you to fill in a second questionnaire to see what sort of sleep problem you have.**
- **You may be contacted based on your answers to this questionnaire if we feel you would benefit from being part of our trial of a non-drug treatment for insomnia.**

The detail below describes the study for your information.

#### About the study

Several general practice clinics in the Auckland area have been involved in this study allowing us to send out the first questionnaire about sleep. Questionnaires have been sent out to people aged between 16 and 75 years old belonging to these clinics. Sleep study flyers and posters have also been available in practices.

Those who indicated on this first questionnaire that they have significant problems with sleep have been asked to fill in a second questionnaire which tells us about the type of sleep problem you may have. The questionnaire also asks some personal questions for example about your living situation, feelings (eg. anxiety, depression, fatigue) and drug use (prescribed medications, alcohol, cigarettes and illicit drugs). This is to help us find people who have poor sleep that is not caused by an identifiable cause. It also helps us to monitor changes that may occur due to the effect of treatment (eg. feeling less anxious).

If this second questionnaire shows that you have poor sleep but have no other medical or mental health problem causing this (such as severe snoring or depression) we call your condition 'Primary Insomnia'.

***Primary Insomnia: poor sleep, bad enough to cause impairment in functioning the next day, that is not due to any other medical or mental health problem.***

- **If your questionnaire does not show 'Primary Insomnia' → thank you for your participation. You will not be contacted further by our team. However, as your initial questionnaire showed you are having difficulty with sleep, you may want to discuss this with your family doctor. They will not contact you automatically, even if you have asked that the questionnaire results are forwarded to them.**

- **If you have 'Primary Insomnia'** → we would like to see if you are suitable for our study.

**If you have 'Primary Insomnia'** A researcher will phone you and ask you several brief questions about your health and occupation to make sure that it is safe for you to participate. For example, you will be asked if you experience any chest pain, shortness of breath or fainting episodes. If you have a job where being tired is risky such as being a bus driver or being a surgeon we will ask you further questions about this.

If you are fit and well we would like to include you in our study testing two different treatments for insomnia.

### **If I am invited to be in the study and I would like to be involved, what happens next?**

If you fall into any of the following exclusion categories, further participation is not required. Thank you for your participation up to this point:

- 1) You are unable to read or write English
- 2) You have a major medical condition (e.g. cancer) or a degenerative neurological condition (e.g. dementia)
- 3) You have a major mental illness e.g. major depression, major anxiety, schizophrenia or bipolar disorder
- 4) You have another diagnosed sleep problem (e.g. sleep apnoea)
- 5) Use of any sleeping pills in the month before the study starts (however, you can stop these and be part of the study)
- 6) You have drug or alcohol abuse or dependence
- 7) You are pregnant, breastfeeding or gave birth less than 6 months ago
- 8) You are a shift worker

### ***If you do not fall into any of the above categories we would like you to take part in the study:***

- If your completed questionnaire shows you have 'Primary Insomnia' you will be phoned by a researcher to make an appointment to discuss the study either at the university or at a local café if this is more convenient for you.
- At this appointment with one of the researchers the study will be explained to you and you will have the opportunity to ask questions. You will be asked to sign a consent form. This is a record for us that you are happy to be involved. Even though you may have signed this form, you may pull out of the study at any time.
- You will be asked to wear a small wristwatch like device called an 'Actiwatch'. This is a miniaturised, computerised device to monitor and collect data generated by movements. The Actiwatch is worn continuously for a 2 week period at the start of the study and after 6 months. You will also need to fill out a sleep diary during these times. The Actiwatch can be worn during almost all activities including in the shower.

This device gives us an accurate idea of the amount of time spent asleep and awake.  
The information collected by the Actiwatch is downloaded into a computer for analysis.

- After you have worn your Actiwatch and filled out the sleep diary for two weeks you will need to attend an appointment at the university.
- You will be asked some questions about sleepiness and fatigue and you may be asked questions about things like how many accidents you have had recently and how many days off work you have had due to tiredness. Your blood pressure, height, weight and pulse rate will be taken. A brief physical examination (you do not need to remove your clothes) will be performed by the qualified researcher (a doctor) to make sure you are otherwise well and do not have a disorder called obstructive sleep apnoea (OSA) which can cause insomnia. You will be referred to your GP if it is thought this is the case.

- You will then be given instructions regarding the treatment you are to receive. You will need to follow these instructions each night until your second appointment at the end of the study. There are two treatments. Neither treatment involves medication. You will not be told specifically which treatment group you are in as it is important no one knows who is in which group until all the results have been collected at the end of the study.
- This first visit will take between 1 and 1.5 hours. Your answers will be written down but you will not be recorded or taped. However, the investigator may be tape recorded whilst explaining your treatment to you.
- You will need to come to an appointment two weeks after you have started the treatment and asked a few simple questions and your blood pressure and pulse rate will be checked. This will take about 30 minutes. After this, each night, you continue to follow the instructions you were given.
- You will be sent a reminder notice in the mail after 3 months reminding you of your study instructions. After 6 months you will be asked to fill out a sleep diary and wear the Actiwatch for two weeks before attending an appointment which will be very similar to the first appointment. It will take about an hour. At this time you will be told which group you are in and you will also be given details of the other treatment which you may try if you want to.

---

### **What are the benefits of being part of the study?**

Your sleep and how you feel after a night's sleep may improve.

You may see improvements in your health and wellbeing such as:

- less fatigue and sleepiness
- improved concentration and work performance
- less moodiness and anxiety
- improved weight, blood pressure and heart rate
- less injuries and accidents
- less time off work due to fatigue
- reduced need for caffeine, alcohol and drugs

---

### **What are the risks or inconveniences of being part of the study?**

You may find there is no change in your sleep

You may get even less sleep than usual

If you are temporarily feeling more tired this may put you at risk of injuries and accidents

You may need to break longstanding habits or change your routines

### **Results**

You may request that the answers to the questionnaires are sent to your doctor with whom you can then follow up your concerns. *Please indicate this on your consent form.* There is a delay from when the questionnaires are received and when your GP will receive a copy.

It is important to remember that in certain situations (e.g. applying for life insurance, health insurance or other insurances) insurance companies may ask permission to have access to your GP's (family doctor's) records. Some of the information we have requested may have implications for your life insurance (or other insurances). Note: You always have to sign a consent form before the insurance companies have access to these records, however insurance may not be granted if you have not allowed full access to your medical record.

If the results are not sent to your doctor he or she will not know from us that you have taken part in the study.

### **Payment**

There is no payment for taking part in this study. However, you will go into the draw to win Westfield vouchers on completion of the questionnaire.

### **Questions**

More information on this study can be obtained by contacting Dr Karen Falloon XXX or by emailing [sleepstudy@auckland.ac.nz](mailto:sleepstudy@auckland.ac.nz).

### **Participation**

Your participation is entirely voluntary (your choice). You do not have to take part in this study, and if you choose not to take part this will not affect your future medical care or treatment.

You may stop being a part of this study at any time.

### **Advocacy**

This is a free service provided under the Health and Disability Commissioner Act.

If you have any queries or concerns regarding your rights as a participant of this study you may wish to contact an independent Health and Disability Advocate, telephone: 0800 555 050, free fax: 0800 2787 7678, or email: [advocacy@hdc.org.nz](mailto:advocacy@hdc.org.nz).

### **Confidentiality**

No material which could personally identify you will be used in any reports on this study.

Questionnaires and interview transcripts will be kept securely by the University of Auckland researchers during the study and by the principal researcher Professor Bruce Arroll at the University of Auckland for a period of seven years after the completion of the study. After this time the records will be destroyed in a confidential manner.

### **Results**

Results of the study will be available about 18-24 months following your participation. If you have requested, your results will be sent to you and/or your doctor.

The outcome of the study as a whole will be reported and sent to the general practice clinics which participated in the study, to medical journals for publication and presented to conferences of health professionals.

### **Statement of Ethical Approval**

This study has received ethical approval from the Northern X Regional Ethics Committee on 24/4/08 until review on 24/04/13.

Reference number NTX/08/02/003

### **ACC Compensation**

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement for costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators.

If you have any questions about ACC, contact your nearest ACC office or the investigator.

### **Funding**

Funding for this research has been provided through a grant from the Health Research Council of New Zealand and the Royal New Zealand College of General Practitioners Auckland Faculty Board charitable trust.

*Please feel free to contact the researchers if you have any questions about this study - Dr Karen Falloon is the primary contact person*

*Thank you for your participation*

**Principal Researcher**

**Professor Bruce Arroll MBChB, FRNZCGP, PhD**  
Head of Department, Department of General Practice and Primary Health Care  
University of Auckland  
Private Bag 92019  
Auckland  
ph: 09 3737599 ext.XXX fax: 09 3737624 email:

Professor Arroll has a 20 year history of research in primary care. He has over 200 publications in the medical literature. As well as studies on insomnia he currently has a major funded trial on the use of 2 screening tools for depression.

**Co-Researchers**

**Dr Antonio Fernando MD, FRANZCP**  
Psychiatrist and Sleep Specialist  
School of Medicine  
University of Auckland Ph 09 3737599 ext XXX

Dr Fernando works as a psychiatrist with Auckland District Health Board. He has extensive experience in the area of sleep medicine and runs the only Insomnia-dedicated clinic in New Zealand.

**Dr Karen Falloon MBChB, FRNZCGP**  
Honorary Research Fellow  
Department of General Practice and Primary Health Care  
University of Auckland Ph 09 3737599 ext.XXX

Dr Falloon graduated Auckland Medical School in 2001. She completed her general practice training in 2009 becoming a fellow of the Royal New Zealand College of General Practitioners (FRNZCGP). Currently Dr Falloon has a Health Research Council Clinical Research Training Fellowship and is undertaking this study as her doctoral research project.

## Appendix J: Sleep Disorder Diagnosis and Exclusion Guide

| Diagnosis  | Questions  | Definition used for diagnosis  |
|------------|--|--|
| Depression | <p><b>PHQ-9: Over the <u>last 2 weeks</u>, how often have you been bothered by any of the following problems?</b><br/> <i>Please circle the number that applies to you including not at all where that is the case</i></p> <p>(R. L. Spitzer et al., 1999)</p> | <p>⇒ Excluded and coded as depression if PHQ-9 score <math>\geq 9</math></p> |



|                    |  |   |
|--------------------|--|---|
| Anxiety            | <p><b>GAD-7: Over the last 2 weeks, how often have you been bothered by any of the following problems? Please circle the number that applies to you including not at all where that is the case.</b></p> <p>(Kroenke et al., 2007)</p> | ⇒Excluded and coded as anxiety if GAD ≥ 8                               |
| Alcohol Dependence | <p><b>CAGE:</b></p> <p>(Ewing, 1984)</p>   | ⇒Excluded if ≥2 (used to indicate potential alcohol problem/dependence) |

|  |  |   |
|--|--|---|
| <p>Menopausal Hot Flushes</p>                  | <p><b>a.</b> Are you menopausal/postmenopausal?<br/> <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p><b>b.</b> If <b>Yes</b>, Do you experience hot flushes?<br/> <input type="checkbox"/> No <input type="checkbox"/> Yes.</p> <p style="padding-left: 40px;">i. If <b>Yes</b>, How many times per night do you awaken due to hot flushes?<br/> _____</p> <p style="padding-left: 40px;">ii. If <b>Yes</b>, Do these significantly affect your sleep?<br/> <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p style="padding-left: 40px;">iii. If <b>Yes</b>, How many nights per week do you experience insomnia due to the hot flushes? _____</p> <p><b>c.</b> [Do you feel that your poor sleep started with menopause (regardless whether or not you get hot flashes that affect your sleep)? <input type="checkbox"/> No <input type="checkbox"/> Yes]</p>  | <p>⇒ Coded as Insomnia due to Menopause if Yes to a+bii and ≥3 nights per week insomnia due to hot flushes</p>                            |
| <p>Obstructive Sleep Apnoea Syndrome (OSA)</p> | <p><b>a. During the <u>past month</u>, how often have you had trouble sleeping because you cough or snore loudly</b></p> <p style="padding-left: 40px;">3. Not during the past month <input type="checkbox"/></p> <p style="padding-left: 40px;">4. Less than once a week <input type="checkbox"/></p> <p style="padding-left: 40px;">5. Once or twice a week <input type="checkbox"/></p> <p style="padding-left: 40px;">6. Three or more times a week <input type="checkbox"/></p> <p><b>b. Do you:</b></p> <p style="padding-left: 20px;">iv. Snore very loudly - <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p style="padding-left: 20px;">v. Get morning headaches - <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p style="padding-left: 20px;">vi. Have a dry mouth upon awakening? <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p><b>c. Do you wake with breath holding, gasping or choking?</b> <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p><b>d. Have you ever been told you have loud snoring or “stop breathing” /pause breathing while you are asleep?</b> <input type="checkbox"/> No <input type="checkbox"/> Yes → please state which</p> | <p>⇒ Coded as SDB/OSA and excluded if:<br/> Ticked a4, bi+bii+biii, c=yes, or d=yes (stop breathing).<br/> Also excluded if ESS&gt;10</p> |

|   |   |   |
|---|---|---|
| <p>Restless Legs Syndrome (RLS) or Nocturnal leg cramps</p> | <p><b>a. At night or in the evening, do you get unpleasant sensations in your legs (urge to move, aches, pains, creeping sensations) <u>which affect your sleep</u>?</b><br/> <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p><b>b. Does the urge to move or the unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting?</b><br/> <input type="checkbox"/> n/a <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p><b>c. Are these sensations partially or totally relieved by movement, rubbing or walking?</b><br/> <input type="checkbox"/> n/a <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p><b>d. On average, how frequently do these sensations disturb your sleep?</b><br/> <input type="checkbox"/> Three or more nights per week<br/> <input type="checkbox"/> less than three nights per week</p>  | <p>⇒Coded as RLS/Nocturnal leg cramps and excluded if a+b+c+ three or more nights per week in questionnaire</p>   |
| <p>Delayed sleep phase disorder</p>                         | <p><b>a. Do you have difficulty falling asleep before 1am and a difficulty awakening at the desired time or at a socially acceptable time (that is, in time for school or work to start)?</b><br/> <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p><b>b. In the weekends or on holiday (when you can sleep when you want) do you go to sleep late (after 1am) and wake up in the late morning or afternoon and feel like you have had a good night's sleep?</b><br/> <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p><b>c. Do you have difficulty staying awake in the early evening (6-9pm)?</b><br/> <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p><b>d. Do you typically wake between 2-5am in the morning?</b><br/> <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p><b>e. If you can follow your own sleep schedule (e.g. on holidays or at weekends), do you go to bed before 9pm and wake before 5am and feel like you have had a good night's sleep?</b><br/> <input type="checkbox"/> No <input type="checkbox"/> Yes</p> | <p>⇒Excluded if<br/> A = yes + b=yes<br/> Or<br/> C = yes + d=yes +e=yes</p> <p>Check written sleep timing to ensure they confirm probably delayed or advances sleep phase pattern. If not, clarify with patient.</p> |

|               |  |   |
|---------------|--|---|
| Sleep walking | <p><b>a. Do you sleep walk?</b> <input type="checkbox"/> No (go to Q15) <input type="checkbox"/> Yes</p> <p><b>b. Did this start before you were a teenager?</b> <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p>iv. When you are walking in your sleep is it difficult for others to wake you up?<br/><input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p>v. Do you have trouble remembering the episode(s) of sleep walking?<br/><input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p>vi. Do these sleep walking episodes occur during the first third of your time asleep?<br/><input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p><b>c. Does your sleep walking affect you or people around you in any way?</b><br/><input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p>If <b>Yes</b>, in what way?</p> <p><b>d. Is your sleep walking severe enough to affect your sleep?</b> <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p><b>e. How often do you sleep walk?</b> <input type="checkbox"/> only occasionally<br/><input type="checkbox"/> at least weekly<br/><input type="checkbox"/> three or more times per week<br/><input type="checkbox"/> not sure</p> | ⇒Coded as Insomnia due to Sleep Walking if Yes responses to:<br>a+d+e |
| Bruxism       | <p><b>a. Do you grind your teeth or clench your teeth when asleep?</b><br/><input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p><b>b. If Yes, Do you have:</b></p> <p>iv. Abnormal wear of your teeth? <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p>v. Sounds associated with teeth grinding? <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p>vi. Jaw muscle discomfort? <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p><b>c. If you answered Yes to either a or b is your teeth grinding severe enough to affect your sleep?</b><br/><input type="checkbox"/> No <input type="checkbox"/> Yes</p>  | ⇒Coded as Insomnia due to Bruxism and excluded if affects sleep.      |

|   |   |  |
|---|---|--|
| Nightmares                                    | <p><b>d. During the <u>past month</u>, how often have you had trouble sleeping because you have had bad dreams?</b></p> <p><b>e.</b> Not during the past month <input type="checkbox"/><br/> Less than once a week <input type="checkbox"/><br/> Once or twice a week <input type="checkbox"/><br/> Three or more times a week <input type="checkbox"/></p> <p><b>f. Do you ever have recurrent severe nightmares that wake you up?</b><br/> <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p>If <b>Yes</b>, how often does this happen?<br/> Not during the past month <input type="checkbox"/><br/> Less than once a week <input type="checkbox"/><br/> Once or twice a week <input type="checkbox"/><br/> Three or more times a week <input type="checkbox"/></p> | ⇒Coded as Insomnia caused by nightmares if three or more times per week on either question |
| Night panics                                  | <p>Do you wake up in the middle of the night having an anxiety or panic attack? (palpitations, pounding heart, difficulty breathing, shaking, feeling faint?)<br/> <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p>If <b>Yes</b>, how often does this happen? _____</p>   | ⇒Coded as Insomnia caused by panic attacks and excluded if Yes and ≥three times per week.  |
| Drug Use (Stimulant-Dependent Sleep Disorder) | <p><b>a. Have you ever taken any of the following drugs to get high, to feel better or to change your mood over the past 3 months?</b><br/> <input type="checkbox"/> No<br/> <input type="checkbox"/> Yes ➔ indicate below and write how often you use them (i.e daily, weekly, monthly)</p> <p><b>b. Do you think the use of drugs is affecting your sleep either when you are taking them or after you stop taking them?</b><br/> <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p><b>c. Do you think the use of these drugs affects your quality of sleep? (while you are using them or after you stop taking them)</b><br/> <input type="checkbox"/> No <input type="checkbox"/> Yes</p>   | ⇒Coded as Drug Use and excluded if a, b, or c  |
| Shift Work                                    | <b>Are you a shift worker?</b> <input type="checkbox"/> No (go to Q6) <input type="checkbox"/> Yes  | ⇒Excluded if a shift worker  |

## Appendix K: ReFRReSH Trial Consent Form



### Participant Consent Form

Effectiveness of a non-drug treatment for primary insomnia

| I wish to have an interpreter.   | Yes | No    |
|--|-----|-------|
| E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero                               | Ae  | Kao   |
| Ka inangaro au i tetahi tangata uri reo.   | Ae  | Kare  |
| Au gadreva me dua e vakadewa vosa vei au   | Io  | Sega  |
| Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.                                     | E   | Nakai |
| Out e mana'o ia i ai se fa'amatala upu   | Io  | Leai  |
| Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika | Io  | Leai  |
| Oku ou fiema'u ha fakatonulea  | Io  | Ikai  |

- I have read and understood the information sheet dated 28 November 2008 for volunteers taking part in the study designed to test the effectiveness of a non-drug treatment for primary insomnia. I have had the opportunity to discuss this study. I am satisfied with the answers I have been given.
- I have had the opportunity to use whanau support or a friend to help me ask questions and understand the study.
- I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time and this will in no way affect my continuing health care.
- I consent to the collection of my details in the study questionnaires and to the brief physical exam (clothed) that will be performed at the start of the study to check that I am fit to take part in the study.
- I have read and understand the risks and benefits of the study and am especially aware of the safety precautions regarding sleepiness.
- I understand that my participation in this study is confidential and that no material which could identify me will be used in any reports on this study.
- I have had time to consider whether to take part.
- I know who to contact if I have any questions about the study.

**Participant Consent Form**  
**Effectiveness of a non-drug treatment for primary insomnia**

Please fill in all parts of this consent form

1) I, \_\_\_\_\_(full name) I have read the study information and consent form and hereby consent to take part in this study. I am aware that the exception to confidentiality will be if the interviewer has significant concern about the safety of myself or others:

Date:

Signature:

2) I understand what is involved in actigraph measurement and consent to having this performed on myself:

Date:

Signature:

3) I wish to receive the final study results    YES / NO

4) I agree to the information from the questionnaire going into my medical records    YES / NO

Researchers

Professor Bruce Arroll:    ph 09 3737599 ext. XXX

Dr Antonio Fernando

Dr Karen Falloon (Project manager) XXX    sleepstudy@auckland.ac.nz

Project explained by:    Karen Falloon

Project role: researcher

Signature:

Date:

## Appendix L: Actiwatch Handout



**The Actiwatch**

Note: If you take your Actiwatch off for a shower, please make sure you record this on your sleep diary and put it back on straight after your shower.

Worn continuously by you for two weeks this device provides important information on your sleep/wake patterns to supplement the information you record in your daily sleep diary.

The Actiwatch is worn on the non-dominant hand 24-hours per day, 7-days per week.

- The Actiwatch materials are polyurethane/polyester (case), titanium (frame and battery cover) and nylon (wristband).
- Although the Actiwatch is watertight we would advise that you remove the Actiwatch for activities such as showering and submersion in water. However, please remember to put your Actiwatch back on immediately after showering etc (and please record the times the Actiwatch is off your wrist).
- The device will tolerate normal daily experiences such as shower, spa(hot tub), swimming, skiing, rain, household chores etc.
- Use extreme care to avoid scratching the metal surface of the device as scratches can cause the watch to leak (this can be avoided by not taking the strap off the watch).
- Cleaning: The Actiwatch has been cleaned prior to your use. Unless you spill anything on it, cleaning by yourself is not usually necessary. If you do need to clean the Actiwatch, the instructions are provided below.

The Actiwatch and band may be cleaned by using a cloth moistened with a mild detergent and warm water (see instructions below). Do not use bleach, alcohol, cleaning solutions containing alcohol or any strong household cleaners.

### Cleaning the Actiwatch band:

1. Remove the band from the device
2. Hand wash the band in warm water with a mild detergent. Rinse.
3. Gently dry with a paper towel or soft cloth, or air dry.

### Cleaning the Actiwatch device: *Caution! Do not clean this device while the battery cover is off.*

1. Clean with the battery cover on
  2. Wet a corner of a clean cloth with warm water. Add a drop or two of mild detergent to the wet cloth and gently wipe the actiwatch device. Wet another corner with warm water and wipe away soap residue.
  3. Gently dry with a paper towel or soft cloth.
  4. Mount the Actiwatch back on the clean band.
- If you notice any unexplained changes in the performance of this device, if it is making unusual or harsh sounds, if it has been dropped or mishandled, or if the enclosure is broken, discontinue use and contact the investigators ([sleepstudy@auckland.ac.nz](mailto:sleepstudy@auckland.ac.nz)).
  - Operation of the Actiwatch may be adversely affected by:
    - operation of high frequency (diathermy) equipment
    - Defibrillators or short wave therapy equipment
    - Radiation (e.g., x-ray, CT)
    - Magnetic fields (e.g., MRI)
  - Do not use this device in the presence of a flammable anaesthetic mixture or in the presence of nitrous oxide



## Appendix M: Sleep Diary and Instructions

### REFRESH Trial

|   | Example                |  |  |  |  |  |  |  |
|---|------------------------|--|--|--|--|--|--|--|
| 1. Yesterday I napped from ____ to ____ (note the times of all naps)                            | 1:50 to<br>2:30pm      |  |  |  |  |  |  |  |
| 2. Last night, I went to bed at ____ o'clock<br>3. I then turned the lights off at ____ o'clock | 11:15pm<br><br>11:30pm |  |  |  |  |  |  |  |
| 4. After turning the lights out, I fell asleep in ____ minutes.                                 | 40min                  |  |  |  |  |  |  |  |
| 5. My sleep was interrupted ____ times (specify number of nighttime awakenings).                | 3                      |  |  |  |  |  |  |  |
| 6. My sleep was interrupted for ____ minutes (specify duration of <u>each</u> awakening).       | 10<br>5<br>45          |  |  |  |  |  |  |  |
| 7. In the morning, I woke at ____ o'clock (specify the time)                                    | 6:15am                 |  |  |  |  |  |  |  |
| 8. In the morning, I got out of bed at ____ o'clock (specify the time)                          | 6:40am                 |  |  |  |  |  |  |  |
| Times the watch was off e.g. for showering (specify time period)                                | 6.50am<br>to<br>7.15am |  |  |  |  |  |  |  |

**REFRESH Trial**  
**Sleep Diary Instructions**

Adapted from Morin CM. *Insomnia: Psychological Assessment and Management*. New York, New York: The Guilford Press; 1993. Reprinted with permission. Not available for digital copy.

# Appendix N: Physical Examination

## PHYSICAL EXAMINATION

Code:

BP:                      Pulse:

Height:                      Weight:                      BMI:

Exclude if  
BMI>35

Neck circumference:

Exclude if  
circumf >42cm

Face:                      Normal(ish)                      mid-face hypoplasia                      Retrognathia/micrognathia

Exclude if  
Hypoplasia or  
retro/micrognathia

Nasal deformity/obstruction:                      none                      slight                      significant

Exclude if  
significant

(Mallampati et al., 1985)

Exclude if  
Tonsillar grade 2 or 3

Exclude if  
Class III or IV

Tonsils/palate: normal                      abnormal

Cardiac examination: normal                      abnormal \_\_\_\_\_

Chest examination: normal                      abnormal \_\_\_\_\_

Other \_\_\_\_\_

## Impression

- Cannot exclude medical co-morbidity as alternative cause for insomnia
- Moderate or high probability of Obstructive Sleep Apnoea or Sleep Disordered Breathing
- Appears medically fit for trial participation

Examination performed by:

Date:

## Appendix O: Baseline Questionnaires



### i) Baseline Questionnaire

How long have you had problems sleeping?:.....

*Please circle your responses below:*

1. Please rate the current (i.e., last 2 weeks) **SEVERITY** of your insomnia problem(s):

**Insomnia Severity Index** (Morin, Belleville, Belanger, & Ivers, 2011)

2. How likely are you to doze off or fall asleep in the following situations, in contrast to just feeling tired?:

would never doze = 0  
 slight chance of dozing = 1  
 moderate chance of dozing = 2  
 high chance of dozing = 3

| Situation (Epworth Sleepiness Scale copyright © MW Johns 1990-1997) | Chance of dozing (0-3) |
|---|------------------------|
| Sitting and reading   |                        |
| Watching tv   |                        |
| Sitting, inactive in a public place (eg theatre or meeting)         |                        |
| As a passenger in a car for an hour without a break                 |                        |
| Lying down to rest in the afternoon when circumstances permit       |                        |
| Sitting and talking with someone                                    |                        |
| Sitting quietly after a lunch without alcohol                       |                        |
| In a car, while stopped for a few minutes in the traffic            |                        |

Office use  
only:ESS=

3. We are interested in the extent that you have felt **fatigued** (tired, weary, exhausted) over the last **two weeks**. We **do not** mean feelings of **sleepiness** (the likelihood of falling asleep). Please circle the appropriate response in accordance with your average feelings over this two-week period:

i. Was fatigue a problem for you?

Not at all             Moderately             Extremely

ii. Did fatigue cause problems with your everyday functioning (e.g., work, social, family)?

Not at all             Moderately             Extremely

iii. Did fatigue cause you distress?

Not at all             Moderately             Extremely

iv. How often did you suffer from fatigue?

0 days/week       1-2 days/week       3-4 days/week       5-6 days/week       7 days/week

v. At what time(s) of the day did you typically experience fatigue? (Please tick box(es))

Early morning       Late afternoon   
 Mid morning       Early evening   
 Midday       Late evening   
 Mid afternoon

vi. How severe was the fatigue you experienced?

Not at all             Moderate             Extreme

vii. How much was your fatigue caused by poor sleep?

Not at all             Moderately             Entirely

4. Over the last 2 weeks, how often have you been bothered by any of the following problems?  
*Please circle the number that applies to you including not at all where that is the case*

PHQ-9 (R. L. Spitzer et al., 1999)

**NB. If you have had thoughts that you would be better off dead or of harming yourself your GP will automatically be notified – it is advised that you speak to your GP about this**

PHQ-9 =

5. Over the last 2 weeks, how often have you been bothered by any of the following problems?  
*Please circle the number that applies to you including not at all where that is the case.*

GAD-7 (Kroenke et al., 2007)

OFFICE USE ONLY:  
10. Sleep Quality (PSQI) =

**Sleep diary information:** (nb all time periods in minutes)

- 11a.i. 'Overall' Time in bed .....
- 11a.ii. 'TIB' .....
- 12a. WASO.....
- 13a. Total sleep time.....
- 14a. SOL.....
- 15a. i. Sleep efficiency (estimated total sleep time/time in bed x 100%) .....
- 15a. ii Bedtime efficiency.....

**Actigraphy information**

- 11b.i. Time in bed/rest int:
- 11b.ii. 'TIB'/sleep int:
- 12b. WASO:
- 13b. Total sleep time:
- 14b. SOL
- 15b. Sleep efficiency:.....

**Physiological measures:**

- 16. weight (kg):..... 17. Height (m):..... 18. BMI (wt/hxh):.....
- 19. Heart rate (resting, seated, average of 2 readings):.....
- 20. Blood pressure (resting, seated, average of 2 readings):.....

**ii) Supplementary Baseline Questionnaire**

What treatments do you know of for insomnia? (please list all you can think of):

Which of these treatments have you tried?

iii) Safety/Harms Questionnaire

**Insomnia Treatment Study**

**Baseline**

Male or female:

Phone number:

Age:

1) How many motor vehicle crashes have you been involved in during the last six months?.....  
 In how many of these were you the driver?.....

2) How many physical injuries *where you needed medical attention* have you had in the last six months?.....

3) How many physical injuries *where you did not need medical attention* have you had in the past six months?.....

4) In the last six months have you had (please circle) :

- a. Worsening angina?      Yes      No
- b. A heart attack?              Yes      No
- c. A stroke or "mini-stroke"?      Yes      No
- d. Admission to hospital?      Yes      No

⇒ if Yes, what was this for?.....

Office use only:  
If Yes=excl

5) In the last two weeks have you fallen asleep or felt very close to this whilst: (please circle)

- Being the driver in a car (even if stopped at the lights)?      Yes      No
- Operating machinery?      Yes      No
- Cooking?      Yes      No
- Looking after children?      Yes      No
- Riding a bike?      Yes      No

Any other situation that worried you or that may have been unsafe had you fallen asleep?  
 Yes      No

What situation:.....

Office use only:  
If Yes=check  
ESS

Office use only:

|                | Baseline – Week 0 | Week 2 | Week 24 |
|----------------|-------------------|--------|---------|
| Resting pulse  |                   |        |         |
| Blood pressure |                   |        |         |

Office use only:  
Place in opaque envelope, forward to Angela.



## Appendix P: Good Sleep Guide

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### GOOD SLEEP GUIDE

Many aspects of our lifestyle, bed time environment and routines can be changed to improve our sleep pattern. Sometimes there may be a simple solution to a person's sleep problem, such as stopping drinking excessive amounts of coffee. However, for most people it is a case of making the most of all of the good sleep practices in a consistent manner to make sure that you are a bit better prepared for sleep each night.

✓ **Limit use of caffeine, alcohol, cigarettes and other substances that can affect sleep.**

*Caffeine and nicotine are stimulants and can ruin your sleep quality*

*Caffeine should be discontinued 4-6 hours before bedtime. Limiting yourself to a cup in the morning is best. The impact of caffeine can vary across individuals but caffeine does tend to stay in the system in significant amounts for a number of hours*

*Although many people claim that smoking makes them relax, nicotine is also a stimulant and should be avoided near bedtime and upon night awakenings*

*The stimulating effects of caffeine and nicotine are particularly detrimental to sleep*

*Alcohol is a depressant and can also worsen your sleep quality. Although it may facilitate sleep onset by making you relaxed and drowsy, it causes awakenings and a change in sleep patterns later in the night. If alcohol must be taken, limit consumption of a glass of wine or beer before or with dinner rather than drinking just before bedtime*

✓ **Do not exercise vigorously within 3-4 hours of bedtime. However, regular exercise during the day can deepen sleep.**

*Also avoid exercising if you awaken at night*

✓ **Avoid heavy meals or spicy food at night as it can interfere with your sleep quality.**

*Make sure you have had enough food to eat so that you are not waking up out of hunger. If necessary, have a light snack before bedtime*

✓ **Minimise noise, light and excessive temperature during the sleep period. Make sure your bed is comfortable.**

*You may like to consider using ear plugs, window blinds, electric blanket, air conditioner, or hot water bottle to make your bedtime environment conducive to sleep*

*Keep your bedroom at a comfortable temperature*

*Turn your clock so that you cannot read the time if you awaken during the night*

*Be sure your pet is not disturbing your sleep*

✓ **Taking a warm bath or having a hot drink (milk) can aid with sleep as a slightly warm body temperature can relax you.**

*However, try to avoid fluids as much as possible in the four to six hours before bedtime if your nights are disrupted by having to get up to go to the toilet frequently*

✓ Use bedroom only for sleep (and/or intimacy). Do not work in the bedroom.

✓ Use a bedtime ritual like light reading (not too exciting and not work-related) to get you into a relaxed mode prior to sleep.

✓ Using some relaxation techniques (soft music, prayer, breathing techniques) before going to bed can make the transition to sleep quicker.

---

## Appendix Q: Safety Handout

### Sleep Study SAFETY CARD

If you are feeling tired or drowsy DO NOT DRIVE or operate machinery

***Here are some signs that should tell you to stop and rest:***

- Difficulty focusing, frequent blinking, or heavy eyelids
- Daydreaming; wandering/disconnected thoughts
- Trouble remembering the last few miles driven; missing exits or traffic signs
- Yawning repeatedly or rubbing your eyes
- Trouble keeping your head up
- Drifting from your lane, tail-gaiting, or hitting a shoulder rumble strip
- Feeling restless and irritable

Avoid driving or operating machinery if: you have had less than 5 hours sleep or between the hours of 2am and 5am (the sleepest hours)

See your doctor urgently if you experience the following:

- Chest discomfort or Shortness of breath
- Dizziness/lightheadedness/faintness
- Weakness on one side of your face or body
- New difficulty with speech
- New or worse feelings of depression or anxiety
- Thoughts of harming yourself or others

***In an emergency or if chest heaviness/pain lasting more than 5 minutes call an ambulance 111***

If you find you start falling asleep at inappropriate times e.g. whilst driving, operating machinery, cooking contact the study coordinator.

## **Appendix R: Drowsy Driving Handout**

### **Avoid Drowsy Driving**

- Get a good night's sleep before you drive
- Avoid alcohol both the night before your trip and during your trip
- Avoid any sedative medications (includes some allergy and cold medications) the night before you drive as they may have lasting effects into the next day
- Travel during non-sleeping hours i.e. avoid nighttime driving
- If you are sleepy-STOP AND REST. Swap drivers, have a brief nap, have a coffee and walk around if you are sleepy. Have a 10-15 minute break every 2 hours of driving
- Drive with a companion and share the driving

**It is the responsibility of the driver NOT TO DRIVE if unfit to drive because of sleepiness**

## Appendix S: Simplified Sleep Restriction Script

### The REFRESH trial – Treatment Script

When we look at your sleep diary we see:

\_\_\_\_\_h in bed

\_\_\_\_\_h asleep

\_\_\_\_\_ sleep efficiency

Normal sleep where someone goes to bed, falls asleep fairly easily, followed by a fairly solid sleep, then wake up and get out of bed promptly = 85-90% efficient (that is, not too much extra time in bed not asleep)

What happens when you have much more time in bed than actually asleep is that sleep can be shallower/poorer quality and more fragmented

We can think of sleep a little like an oil spill:

A big tanker spills a blob of oil in the ocean

You get a big deep blob of oil. If spill containment buoys corral it quickly, it is contained as a deep heavy blob

If the buoys aren't there, what happens is the oil starts to spread and disperse over the surface of the ocean – becoming less deep but spreading further over the surface of the ocean. Eventually as the oil is allowed to spread, it may become so thin that it starts to break up as it spreads out.

If we think of sleep as the oil and the ocean as bedtime, we can see that if we have a certain amount of sleep that our brain needs. If it is allowed to spread out over a long bedtime period it becomes shallower, poorer quality and fragmented.

What we propose to do with this treatment is to set bedtimes and wake up times to corral sleep. To “scoop” it all together so it is more condensed and occurs in a more solid chunk.

The benefits of this are:

- Gaining a regular bedtime schedule – important for helping to form a habit of good sleep (think of how we teach babies to sleep well with consistency – when they go to bed they know it is sleep time). Having a schedule and having a regular wake up time regardless of the previous nights sleep means that if you have had a poor night's sleep but still get up at the same time regardless you are likely to be a bit more tired during the day – when bedtime comes, you will be sleepier waiting until your prescribed bedtime and this additional 'sleep pressure' which has built up means you fall asleep faster, and generally have a deeper sleep as your brain 'sucks up' more quality sleep. So you can see that a poor night's sleep actually feeds into the success of the programme.
- Setting a bed time 'allowance' so that the time in bed more closely matches the amount of time spent sleeping. We are not restricting your sleep at all, but reducing the amount of time spent in bed awake.
- Strengthening the association between the bed and sleep (by reducing the amount of time spent in bed awake).

**In order to make your sleep more efficient and hopefully more refreshing, we propose that for the next two weeks, we attempt to retrain your brain to sleep better.**

We can achieve this by rescheduling your sleep such that lighter sleep or the wake up periods are less and the deep sleep or is longer. This can be done by limiting your total time in bed to approximate your reported total time in sleep.

***A good starting point in improving sleep is to get whatever amount of sleep you are getting right now all in one block and the same time each night***

**What we propose in this treatment regimen is to match the time you spend in bed to the actual amount of time you are spending asleep.**

*For you, according to your sleep diary you are spending on average .....hours in bed but only sleeping for an average of..... This means you have .....hours of awake time in bed.*

***Rising at the same time each day acts as an anchor to hold the sleep pattern in the same position***

***Limiting the time you are allowed in bed to correlate closely with the actual time you are spending sleeping is simple in theory but can be challenging in practice. Some people have a hard time forcing themselves to stay awake in the first phase of treatment. However, those who can stick with it often find it remarkably effective***

*It is easier if you plan what you will do in the extra time you are awake in the evenings.*

***Try to do bedtime reading in a place other than your bed, so that you are not spending time in bed awake. If reading in bed is essential for your bedtime routine, limit it to 10-15 min strictly but still adhere to the prescribed into bed and out of bed times.***

*Think of the initial difficult weeks as a retraining period for your brain to get to know how to sleep deep again. If you limit the time you spend in bed for two weeks, your brain becomes quite thirsty for sleep such that when you allow it to sleep at the appointed time, your brain just soaks in sleep like a dry sponge and will not want to wake up until you get out of bed.*

***We do not expect you to be on a severely shortened bedtime schedule forever –this initial period could be anywhere from one week to several weeks.***

*By following the new schedule every single night you will establish a strong pattern for regular sleep in the future.*

*Bedtime restriction helps the broken bits of sleep to knit together and once this has happened the sleep pattern is able to grow to its correct size for you*

- ***The first week can be quite hard and we cannot minimize that. But for it to work, you need to give this sleep protocol your very best effort.***

Go through the 'instructions for the next two weeks'

**\*Advise 1 extra hour is allowed in bed on the weekend only if absolutely necessary, but no more (and this may slow down the programme a bit).**

Questions? Concerns?

## Appendix T: Baseline Simplified Sleep Restriction Prescription Handout

### The REFRESH trial

The treatment we are proposing for you involves retraining your brain to sleep better and deeper.

- From what you are telling us, you go to sleep around \_\_\_\_\_, stay awake for about \_\_\_\_\_ and only actually sleep for \_\_\_\_\_ hours
- Approximately, you are only \_\_\_\_\_ % efficient which results in very poor quality and unrefreshing sleep.
- Ideally, people should be getting 85-90 % sleep efficiency.

What possibly happens in your sleep is that you “snorkel in the sea of sleep” rather than “scuba diving”. It’s generally better if the snorkeling is limited and the scuba diving is longer. The deeper the sleep, the more refreshed you are. **The actual length is not as important as the depth.** There are a lot of people who feel refreshed even with less than 5 hours of sleep as long as it is deep and uninterrupted.

We know that for a lot of people with insomnia, the balance between sleep and wake is out of kilter and needs to be retrained back into synch so that when you go to bed you fall asleep and sleep solidly and when you wake the next day you feel refreshed. This is what this programme will train your body and brain to do.

- In order to make your sleep more efficient and hopefully more refreshing, we propose that for the next two weeks, we attempt to retrain your brain to sleep better.
- We can achieve this by rescheduling your sleep such that the lighter sleep or the wake up periods are less and the deep sleep is longer.
- This can be done by limiting your total time in bed to approximate your reported total time in sleep.

**Your reported total sleep time is \_\_\_\_\_**

#### Weeks one and two

For the first two weeks of the programme your hours allowed in bed per night is \_\_\_\_\_

As you are only allowed \_\_\_\_\_ hrs in bed per night, what will be an acceptable time to go to bed at night and to get out of bed in the morning for you?

\_\_\_\_\_ time into bed, \_\_\_\_\_ out of bed time

This seems harsh but just think of it as a retraining period for your brain to get to know how to sleep deep again. If you limit the time you spend in bed for two weeks, your brain becomes quite thirsty for sleep such that when you allow it to sleep at the appointed time, your brain just soaks in sleep like a dry sponge and will not want to wake up until you get out of bed.

The first week can be quite hard and we cannot minimize that. But for it to work, you need to give this sleep protocol your very best effort. Previous work has shown that almost all people like you have significant improvement after two weeks with this protocol and that this improves the longer the second phase of the programme is followed.

#### Our instructions for you for the next two weeks:

1. Follow your lights out and get out of bed times prescribed above.
2. Please do not take sleep medication or herbal sleep preparations whilst you are on this trial.
3. Avoid naps as this can affect the effectiveness of the sleep protocol.
4. Try and think of quiet activities you can do in the extra time you are awake in the evenings (i.e., don’t listen to loud music or work on the computer as these type of stimulating activities will wake you up when you want to be winding down.
5. Limit use of caffeine, alcohol, cigarettes and other substances that can affect sleep. Follow the “Good Sleep” Handout.
6. Keep a DAILY SLEEP DIARY for the next two weeks, to record your sleep pattern.
7. Please be careful with driving or operating machines as your coordination can get impaired for the next few days. Please read the accompanying safety card and drowsy driving information.
8. If you have urgent questions, please ring Dr Karen Falloon on XXX.  
If it is non-urgent, please email Karen: [sleepstudy@auckland.ac.nz](mailto:sleepstudy@auckland.ac.nz).

*It is very important that you come back to see us after two weeks to see if there have been effects and to adjust things as necessary*

## Appendix U: Week Three Simplified Sleep Restriction Prescription

### The REFRESH trial

The treatment we are proposing for you involves retraining your brain to sleep better and deeper.

From what you are telling us, you are now going to bed around \_\_\_\_\_, stay awake for about \_\_\_\_\_ (hrs/mins) and actually sleep for \_\_\_\_\_ (hrs/mins). Approximately, your sleep is now \_\_\_\_\_ % efficient.

Ideally, people should be getting around 85-90% sleep efficiency.

Poor sleep efficiency results in very poor quality and unrefreshing sleep.

#### Compared to your sleep two weeks ago:

- Your sleep efficiency is somewhat better/unchanged – further reduction in time allowed in bed is needed
  - Your sleep efficiency is poorer than two weeks ago – further reduction in time allowed in bed is needed
  - Your sleep efficiency is now within the ideal range
  - Your sleep is so efficient that you can now go to bed 30 minutes earlier and you will most likely continue to have good sleep efficiency
- The deeper the sleep, the more refreshed you are. The actual length is not as important as the depth. There are a lot of people who feel refreshed even with less than 5 hours of sleep as long as it is deep and uninterrupted.
  - We can achieve solid, deep sleep by rescheduling your sleep such that the lighter sleep or the wake up periods are less and the deep sleep is longer.
  - This can be done by limiting your total time in bed to approximates your reported total time in sleep.

#### Weeks Three and Four

\_\_\_\_\_ lights out time, \_\_\_\_\_ out of bed time

#### Week Five

Follow the sleep self adjustment schedule flowchart

If SE  $\leq$ 85% then restrict TIB by 30 min  
If SE 85-90% and feeling good during the day no change  
If SE 85-90% and sleepy during the day allow 30min extra TIB  
If SE  $>$ 90% then increase TIB by 30min

Reducing the time allowed in bed may seem harsh but just think of it as a retraining period for your brain to get to know how to sleep deep again. If you limit the time you spend in bed consistently for 1-2 weeks your brain becomes quite thirsty for sleep such that when you allow it to sleep at the appointed time, your brain just soaks in sleep like a dry sponge and will not want to wake up until you get out of bed. As your sleep gets more efficient (going to bed and falling asleep within 30 minutes and night awakenings lasting less than 20 minutes) you will be able to spend more time in bed (by following the flowchart), if your sleep then starts to become less efficient and you are sleeping worse the flowchart will get you to limit the hours in bed again to retrain your brain again into the deep sleep habit.

- For this insomnia treatment to work, you need to give this sleep protocol your very best effort
- Your persistence at following the sleep self-adjustment protocol may mean that you attain **lifelong** refreshing and restorative sleep and all the associated health benefits this brings

#### Our instructions for you for the next two weeks:

1. You are not allowed to be in bed earlier than \_\_\_\_\_ pm/am.
2. You have to be out of bed by \_\_\_\_\_ AM regardless of the length or quality of your sleep that night.
3. Avoid naps as this can affect the effectiveness of the sleep protocol.
4. Limit use of caffeine, alcohol, cigarettes and other substances that can affect sleep.
5. Please be careful with driving or operating machines especially when you feel sleepy or fatigued as your coordination can get impaired. Please read the accompanying safety card and drowsy driving information.
6. After two weeks, follow the 'Sleep Schedule Self-Adjustment Algorithm'
7. If you have urgent questions, please ring Dr Karen Falloon on XXX. If it is non-urgent, please email us: [sleepstudy@auckland.ac.nz](mailto:sleepstudy@auckland.ac.nz).

*It is very important that you follow these instructions over the next six months. The aim is for you to be a good sleeper and to know how to manage your sleep if it becomes poor again. Good sleep has so many health and wellbeing benefits it will be worth giving it your best effort.*



## Appendix V: Simplified Sleep Restriction Handout Given to Control Patients at Trial Conclusion

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### REORGANISATION OF BEDTIME HABITS

The following protocol was used by half of the participants in the REFRESH study. *The results into the effectiveness and any possible harms of this intervention will not be known until all the data from the trial has been collected and analysed.* Having said this, the following protocol is commonly used in a package of treatments for those with insomnia.

The purpose of this treatment is to re-shape your sleep so that it meets your individual needs and develops into a strong night-time pattern. It involves determining how much time you spend asleep on average and setting your bedtime and rising time to closely match this. This means that when you are in bed, most of your time is spent getting a good quality sleep.

Individuals tend to compensate for poor sleep by increasing time in bed hoping to capture as much sleep as possible. However, we know that extra time in bed when you are not asleep can be counterproductive. There are several reasons for this: it can weaken the link that being in bed has with sleeping, it can leave more opportunity for thinking and worrying which can keep you awake, and it can mean that you are going to bed when your brain's natural rhythm is not yet ready for sleep. By reducing the amount of time you are allowed in bed you spend less time in bed awake and more time in bed asleep (increasing your 'sleep efficiency').

#### Mistaken beliefs about what might improve sleep

Spending more time in bed

Going to bed early because you think you should "catch up" on sleep, even when you are not sleepy

Making up for a poor night's sleep by staying in bed longer to compensate

#### Normalising sleep habits

Go to bed when sleepy (as opposed to just feeling tired)

Regular wake up time regardless of the quality of sleep during the preceding night

Avoiding naps

A consistent sleeping schedule helps form a habit of consistent sleep

~

Insomnia is often a mixture of bad and better nights. The first step is to work out how much sleep you are getting at the moment, especially if your pattern is all over the place. Sleep diaries help with this by allowing us to find out the average amount of sleep you are getting.

### Step 1

Fill out the sleep diary for two weeks. Work out how much sleep you are getting each night. Add up the 14 nights of sleep and divide by 14 to get the average amount of nightly sleep.

The average amount of sleep I get is: \_\_\_\_\_

*e.g. 6h*

### Step 2

Using your sleep diary, work out how much time you are spending in bed awake. This includes the time from when you get into bed until you fall asleep, any time awake during the night, and the time from when you wake in the morning until you get out of bed. Add up the nightly amounts over two weeks and divide by 14 to get your nightly average awake time.

The average time I spend awake in bed is: \_\_\_\_\_

*e.g. 3h*

### Step 3

Using the information from steps 1 and 2, work out the average time you are spending in bed by adding the two average values.

Average amount of sleep + average amount of time in bed awake = average time spent in bed

My average time spent in bed is: \_\_\_\_\_

*e.g. 9h*

### Step 4

Calculate your target time in bed. Subtract *half* the average time spent in bed awake from your average time spent in bed.

*e.g. 9h (avg.time spent in bed) – 1.5h (1/2 avg. wake time) = 7.5h (target time in bed)*

Therefore, in this example you would need to allow yourself 7.5h in bed each night. These need to be the same 7.5h each night in order to establish a strong routine.

If your sleep diary shows very few hours of sleep the above calculation can yield a very low target time in bed. You need a certain amount of time in bed so target time in bed is *never set less than 5.5h* at this stage.

My target time in bed allowance is: \_\_\_\_\_

*e.g. 7.5h*

~

It is important to have a regular rising time. This allows your sleep routine to be 'anchored'. It allows you to build up a consistent level of sleepiness during the day and for your body and brain to get into a regular habit.

### Step 5

Choose a time to rise *each and every* morning. This should be a time that is comfortable for you and fits in with your daily demands. For example, you may find that 7am is a good time for you as this may be when you need to get up during the week for work.

My morning wake up time is going to be: \_\_\_\_\_

*e.g. 7am*

~

### Step 6

Calculate your prescribed bedtime.

People go to bed for different reasons. Sometimes people go to bed before they are tired and end up lying awake, or they fall asleep quickly but waken very early. Some people go to bed early because they want to catch up on sleep they have lost on previous nights. Others feel it is simply 'bedtime' or they go to bed because everyone else has gone to bed.

It is important to go to bed when you are sleepy. That is, you are ready to fall asleep rather than just feeling tired or bored. Sleep needs vary considerably from one person to another. Some people are very long sleepers and others need very little sleep in order to function well the next day.

To work out your bedtime for this protocol we use your target time in bed allowance that you have calculated in step 4 and the wake up time that you have calculated in step 5.

Wake up time – target time in bed allowance = bedtime

*e.g 7am – 7.5h = 11.30pm*

~

### Step 7

Keep to your bedtime and rising time prescription for two weeks. Continue to fill out a sleep diary during this time. After two weeks, assess your sleep by thinking about which of the below statements applies to you:

"My sleep has improved and I am happy with how I am sleeping now"

"My sleep has improved a bit but I am still not sleeping that well"

"There has been little or no change in my sleep"

"My sleep has become worse (but I am not more sleepy during the day than before)"

"My sleep has become worse and I am significantly sleepier during the day than before"

"My sleep has improved but I find I am significantly sleepy during the day"

If you fall into this category:

- "My sleep has improved and I am happy with how I am sleeping now"

⇒ Keep your sleep schedule as is and review in two weeks with the 'sleep self-adjustment algorithm'.

If you fall into these categories:

- “My sleep has improved a bit but I am still not sleeping that well”
- “There has been little or no change in my sleep”
- “My sleep has become worse (but I am not more sleepy during the day than before)”

⇒ Reduce your target time in bed so that it is equal to your average nightly sleep plus 30 minutes

e.g. Using the examples shown above this would be:  $6h + 30 \text{ minutes} = 6.5h$  allowed in bed. If rising time was kept the same then bedtime would change to 12.30am.

If you fall into these categories:

- “My sleep has become worse and I am significantly sleepier during the day than before”
- “My sleep has improved but I find I am significantly sleepy during the day”

⇒ Add back 30 minutes to your target time allowed in bed.

e.g. Using the examples shown above this would be:  $7.5h + 30 \text{ minutes} = 8h$ . If rising time was kept the same then bedtime would change to 11pm.

~

### **Step 8**

After following your revised sleep schedule for two weeks, assess your sleep using the ‘sleep self-adjustment algorithm’ and adjust your sleep schedule as directed.

\*One extra hour is allowed in bed on the weekend only if absolutely necessary, but no more (and this may slow down the programme a bit).

**Important:** if bedtime restriction leads to undue sleepiness such that it interferes with your safety with driving/operating machinery or your functioning at work you should immediately add back some time to your bedtime allowance. The safety advice and drowsy driving advice is included in this handout although you are probably already familiar with it.

Some people do not manage to have improved sleep despite following the sort of regimen described above – if this is you, you may want to discuss your sleep problems with your family doctor.

## Sleep Diary

|   |                        |  |  |  |  |  |  |  |
|---|------------------------|--|--|--|--|--|--|--|
|   | Example                |  |  |  |  |  |  |  |
| 1. Yesterday I napped from ____ to ____ (note the times of all naps)                            | 1:50 to<br>2:30pm      |  |  |  |  |  |  |  |
| 2. Last night, I went to bed at ____ o'clock<br>3. I then turned the lights off at ____ o'clock | 11:15pm                |  |  |  |  |  |  |  |
| 4. After turning the lights out, I fell asleep in ____ minutes.                                 | 40min                  |  |  |  |  |  |  |  |
| 5. My sleep was interrupted ____ times (specify number of nighttime awakenings).                | 3                      |  |  |  |  |  |  |  |
| 6. My sleep was interrupted for ____ minutes (specify duration of <u>each</u> awakening).       | 10<br>5<br>45          |  |  |  |  |  |  |  |
| 7. This morning, I woke at ____ o'clock (specify the time)                                      | 6:15am                 |  |  |  |  |  |  |  |
| 8. This morning, I got out of bed at ____ o'clock (specify the time)                            | 6:40am                 |  |  |  |  |  |  |  |
| Times the watch was off e.g. for showering (specify time period)                                | 6.50am<br>to<br>7.15am |  |  |  |  |  |  |  |

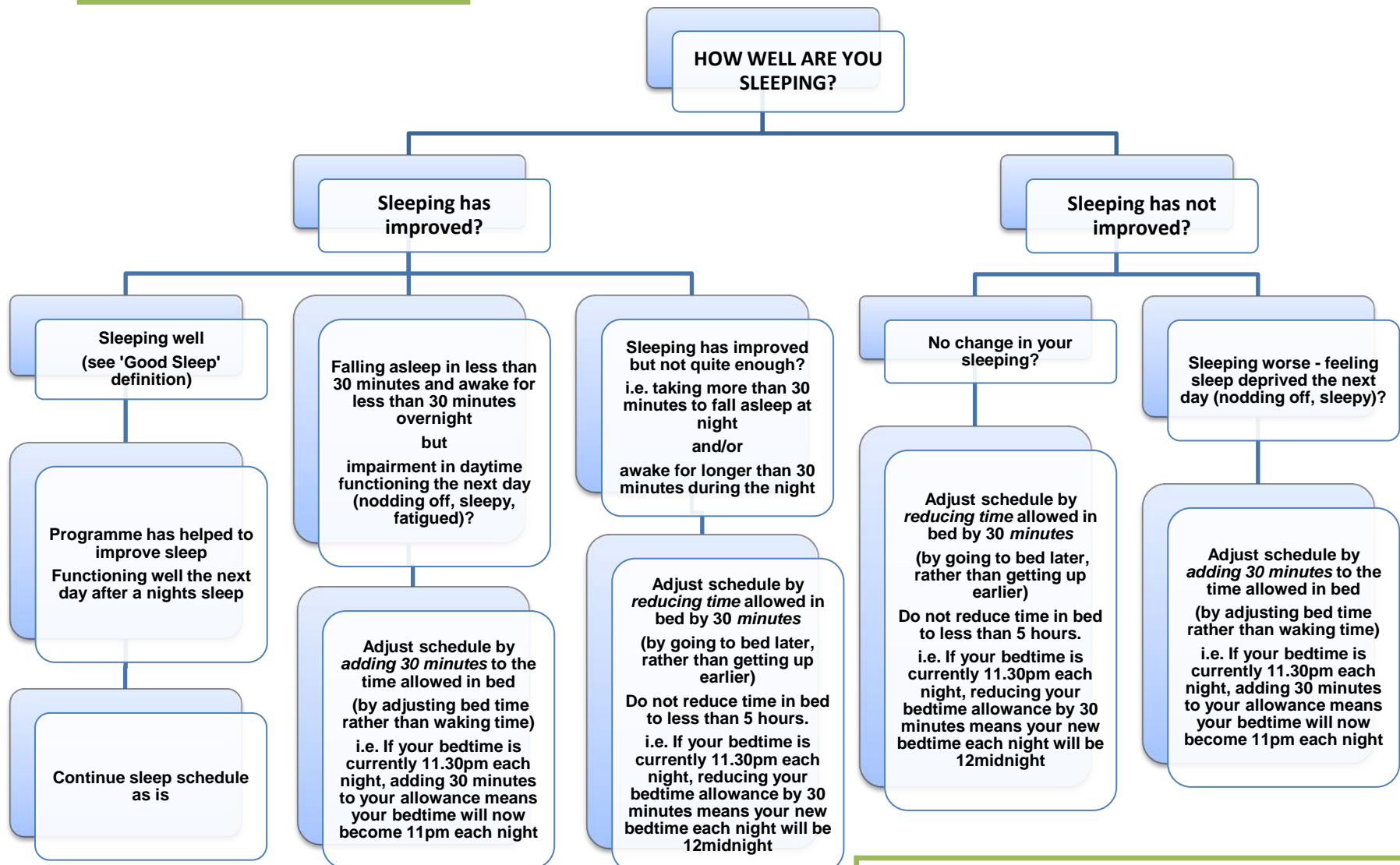
## Sleep Schedule Self-adjustment Flowchart

- Use this flowchart to assess and adjust your sleeping routine for the fortnight ahead
- Do not adjust your sleep schedule more frequently than every fortnight (your body will require time to adjust). Pick a day of the week that you adjust your sleep schedule for the coming fortnight– write it in your diary or calendar so this becomes a routine you don't forget.
- Follow the flowchart below to your new sleep instructions.
- Remember the safety instructions if you are feeling very tired or sleepy
- Changing sleep habits takes commitment – sticking to your sleep rules will give you the best chance of reforming your sleep and gaining long term refreshing sleep.

### **Good Sleep Definition:**

- **Mostly taking less than 30 minutes to fall asleep**
- **Fragmented sleep is not usually a major problem**
- **Usually not waking for longer than 30 minutes during the night**
- **Feeling reasonably refreshed the next day/No major impairment on daytime functioning because of a poor sleep**

Go through this flowchart  
EVERY FORTNIGHT



Do not give up if your results are not immediate – we don't expect they will be for everyone - but we do expect that the majority can gain good sleep.

## Avoid Drowsy Driving

- Get a good night's sleep before you drive
- Avoid alcohol both the night before your trip and during your trip
- Avoid any sedative medications (includes some allergy and cold medications) the night before you drive as they may have lasting effects into the next day
- Travel during non-sleeping hours i.e. avoid nighttime driving
- If you are sleepy-STOP AND REST. Swap drivers, have a brief nap, have a coffee and walk around if you are sleepy. Have a 10-15 minute break every 2 hours of driving
- Drive with a companion and share the driving

**It is the responsibility of the driver NOT TO DRIVE if unfit to drive because of sleepiness**

### General safety advice

If you are feeling tired or drowsy DO NOT DRIVE or operate machinery

#### ***Here are some signs that should tell you to stop and rest.***

- Difficulty focusing, frequent blinking, or heavy eyelids
- Daydreaming; wandering/disconnected thoughts
- Trouble remembering the last few miles driven; missing exits or traffic signs
- Yawning repeatedly or rubbing your eyes
- Trouble keeping your head up
- Drifting from your lane, tail-gaiting, or hitting a shoulder rumble strip
- Feeling restless and irritable

Avoid driving or operating machinery if: you have had less than 5 hours sleep or between the hours of 2am and 5am (the sleepest hours)

See your doctor urgently if you experience the following:

- Chest discomfort or Shortness of breath
- Dizziness/lightheadedness/faintness
- Weakness on one side of your face or body
- New difficulty with speech
- New or worse feelings of depression or anxiety
- Thoughts of harming yourself or others

***In an emergency or if chest heaviness/pain lasting more than 5 minutes call an ambulance 111***

If you find you start falling asleep at inappropriate times e.g. whilst driving, operating machinery, cooking contact your family doctor.



## Appendix W: Sample Size Calculations

Sample size February 2009

. sampsi 0.75 0.5, p(0.8)

Estimated sample size for two-sample comparison of proportions

Test Ho:  $p_1 = p_2$ , where  $p_1$  is the proportion in population 1  
and  $p_2$  is the proportion in population 2

Assumptions:

alpha = 0.0500 (two-sided)

power = 0.8000

$p_1 = 0.7500$

$p_2 = 0.5000$

$n_2/n_1 = 1.00$

Estimated required sample sizes:

$n_1 = 66$

$n_2 = 66$

sampsi 0.8 0.5, p(0.8)

Estimated sample size for two-sample comparison of proportions

Test Ho:  $p_1 = p_2$ , where  $p_1$  is the proportion in population 1  
and  $p_2$  is the proportion in population 2

Assumptions:

alpha = 0.0500 (two-sided)

power = 0.8000

$p_1 = 0.8000$

$p_2 = 0.5000$

$n_2/n_1 = 1.00$

Estimated required sample sizes:

$n_1 = 45$

$n_2 = 45$

## Appendix X: Sleep Diary Analysis Protocol

1. Print out blank 'Sleep Diary Analysis' form from Thesis>chapters>method>trial forms and protocol>baseline visit>researcher
2. Fill in values using completed sleep diary. Start by calculating 'TIB' using the time lights were turned off, to the time of getting out of bed. Convert into minutes. Then enter the time in bed before lights out and, adding this value to the 'TIB' value the 'Overall TIB' can be filled in. Proceed with filling out the rest of the table with the values provided by the completed diary.
3. **Where a night is unusual** e.g. annotated that sick/child unwell or other unexpected event occurred, this night is excluded.
4. **If a value is not completed** e.g. no value for 'time it took to fall asleep' or no value for awakenings or their duration, annotate analysis with a '?' and the value of zero is assigned.
5. **If "many times" or similar descriptor used for number of night time awakenings** use the empiric value of 5 awakenings
6. **If number of awakenings is completed but there is no duration** filled in, each awakening is assigned a duration of 10 minutes.
7. **If "non-stop" or "continuous" descriptors are used instead of numbers** e.g. "awake non-stop" or "non stop awakenings" the empiric value given is 120 minutes
8. **If more than one value is missing** e.g. no SOL and no WASO available or no bedtime or wake up time is given then this night is excluded.
9. **Where a range is given** e.g. "10 to 20 minutes" or "2-3 times" , use the upper value
10. Calculate the average minutes and average hours for each row where this is appropriate.
11. If any nights are excluded, the calculation of averages is adjusted accordingly e.g. dividing the total number of minutes by 13 nights rather than 14 nights if one night is excluded.
12. Derive 'Total sleep time' using: 'TIB' (not 'Overall TIB') minus SOL minus WASO minus TWAK.
13. Calculate sleep efficiency using the formula:  $TST/'TIB' \times 100\%$
14. Calculate bedtime efficiency using the formula:  $TST/'Overall TIB' \times 100\%$
15. Remember to annotate the instructions given to the patient.

### Entering the sleep diary data into the Excel spreadsheet

1. Save the patient's sleep diary data as an Excel spreadsheet – one spreadsheet per subject, saved according to the patient code. Separate tabs are used for baseline/week 3/6 months
2. Open new excel spreadsheet blank template. Enter patient code and sleep diary values. Averages and TST and sleep efficiency/bedtime efficiency should populate with formulae imbedded in blank template. Check that the values entered, especially the averages, TST and efficiencies matches with those entered manually in the sleep diary analysis form.
3. Enter the actigraphy data from actigraph analysis printout.
4. Save Excel spreadsheet using subjects code as name

**\*Enter sleep diary values and actigraphy values into Baseline Questionnaire and ACCESS database**

## Appendix Y: Actigraphy Analysis Protocol

### Downloading data

1. Connect Actireader to designated port on laptop (COM port 4)
2. Open Actiware 5 programme by double-clicking on icon
3. Communications>'retrieve data from actiwatch'
4. Follow through instructions on wizard
5. If error message comes up, the first thing to do is replace battery and try again
6. Once data is read, click on 'launch actigraph automatically' and close wizard
7. Alternatively, close wizard and launch actigraph by clicking on the subject's actigraph on database viewer by clicking on 'new analysis'

### Analysing rest intervals

8. Set 'REST INTERVAL' by clicking on interval>Add interval
9. Set rest interval for each night of the sleep diary using 32 on sleep diary "I went to bed at.." and #8 "I got out of bed at..." ( i.e. 'Overall TIB')
10. If any nights are abnormal/excluded, set and 'EXCLUDED' interval rather than a 'REST' interval
11. Once finished doing this for each night, close the actigraph. Save as new analysis called 'BASELINE' or 'FOLLOWUP' as appropriate

### Viewing and printing statistics

12. View>statistics table>'Sleep' tab
13. To print, close statistic table, select variables to print: Tools>options>statistics tab to check the variables to be included then Tools>options>Print report tab to choose variables to print
14. Close window and click on printer icon to print report

### Important statistics

15. Highlight important statistics as follows:
  - Overall time in bed = 'rest interval duration' average
  - TIB = 'sleep interval duration' average
  - WASO
  - SOL
  - TST = 'sleep time duration'
  - SE
16. Insert these values into back page of 'Baseline Questionnaire'

### Downloading Actigraphy data (text in Excel spreadsheet) *Do this for each individual after their actigraph is analysed.*

17. With database open select: tools>text file export batch>individual export
18. Choose destination: My docs>thesis>Data>patient data>actigraphy>the subject's own folder
19. Follow wizard, save with appropriate subject code.
20. Save a copy of this .csv file onto actigraphy USB then transfer onto uni PC.

### Saving a copy of actigraphy graph

21. With database open select: File>database>backup and save onto actigraphy USE to transfer onto uni PC

## Appendix Z: Blood Pressure Measurement Protocol

- Omron blood pressure monitor kept in the research suitcase
- Connect cuff tubing and power cord to BP monitor console
- Check that the dials are squarely set on “auto” and “single”
- Patient asked to remove clothing that covers the location of cuff placement
- Arm circumference measured and appropriate cuff size selected (see range printed on cuff)
- Secure cuff on arm
- Patient is instructed to relax and rest for 5 minutes prior to the first measurement. Magazines are provided for relaxation.
- Patient should be comfortably seated, legs uncrossed, back and arm supported such that the middle of the cuff on the upper arm is at the level of the right atrium (mid-point of the sternum)
- Advise patient no talking during measurement but to advise if pain from cuff (warn it will get quite tight briefly).
- Turn on using “on/off” button. When the display reads ‘0mmHg’ press “start”. If at any point the reading needs to be interrupted suddenly (e.g. due to pain) press the “stop” button.
- Three recordings taken with five minute interval between each measurement (use the time in between to analyse sleep diary data).
- The average of the last two recordings is used as the final value for both blood pressure and resting heart rate
- If any error codes are reported look in manual kept in lid pocket of research suitcase
- Check that tubing is not kinked by arm position, and reposition as necessary
- Check that the dials are squarely set on “auto” and “single”
- Be familiar with the “Safety/Harms” algorithm for measurements outside the acceptable range. If a patient is outside the range at baseline or 2 week follow up, make a note of the reading and advise patient as per protocol to see their GP. Let Karen know of these instances before the patient leaves.
- Turn the unit off and repack into research suitcase.

# Appendix AA: Baseline, Week Three, and Six Month Assessment Protocols

## Baseline appointment

Print out handouts/questionnaires and researcher forms from:

Thesis>chapters>method>trial forms and protocol>baseline

The safety/harms questionnaire is paper clipped to an envelope which has the date, the participant code and 'baseline' written on it.

- 1) Collect sleep diary and actigraph (*record actigraph as returned*). Give vouchers.
- 2) Hand out questionnaire to be filled in (Baseline and supplementary – the Harms questionnaire is filled out after the BP/P measurements are done)
- 3) Advise that there is still a small chance that the participant does not fit with the criteria required for the study, if this is the case their participation will end here. If looks like they have the type of insomnia we are interested in, they will continue with the study and be given treatment instructions from one of two groups of non-drug treatments for insomnia).
- 4) Work out average (mean)TIB, TST, SOL, WASO, sleep efficiency from the average of the sleep diary data: **Check that inclusion criteria fulfilled**  
*Do this while the participant is filling out the questionnaire and having BP taken*
- 5) Fill in handout with average sleep times, sleep latency and total sleep time
- 6) Check through questionniare to ensure:
  - PHQ-9 < 8
  - GAD-7 <9
  - Query sleepiness if ESS >10
- 7) Take physiological measurements/physical exam ( continue reviewing sleep diary and questionnaire during 15 min BP protocol)
- 8) Get the participant to fill out the Safety/Harms questionnaire after you have filled in their BP and Pulse. You are not to look at this questionnaire so the patient is instructed to complete and place it in the envelope provided and seal with their initials over the closure and some sellotape sealing over this. *This envelope is handed in to Angela Robinson.*
- 9) STOP study if exclusion criteria met
- 10) Group allocation if inclusion criteria met:
  - Randomisation – Ring/text Angela with participant code and she will text back group allocation
- 11) *Start Stopwatch*  
  
Appropriate script read to participant  
Sleep and wake times instructed for those in intervention group  
Go through instructions on handout and safety card/drowsy driving handout (emphasise that this is a general safety education for people with insomnia who aren't getting enough sleep) and make appointment time for next appointment
- 12) Remind to fill in sleep diary for next two weeks
- 13) *Stop stopwatch* and record time taken. Make appointment for next meeting.

### Week three appointment

- Hand in sleep diary – Sleep efficiency calculated for intervention group and new sleep/wake instructions given. Self adjustment algorithm explained and given.
- BP and pulse taken and recorded on blank harms questionnaire form
- Harms questionnaire filled out and sealed in opaque envelope and given to Statistician on safety committee
- Reminder to update contact details if they change
- Remind to continue with sleep behavior instructions
- Advise that reminder letter and brief questionnaire to be sent at 3m (please indicate if you would prefer this to be an email rather than letter).
- Advise that participant will be contacted by investigators to have repeat actigraphy, sleep diary and assessment at 6 months.
- ***Emphasise that two parts to this project – the treatment and the research measurements- even if you don't follow instructions, the most important thing to do is to come back for the research recordings.***

### Six month outcomes

- Initiate contact with participants at approximately 5 months to arrange an appointment to collect actigraph and sleep diary for 2 week recording.
- Appointment booked  
Make appointment for outcomes measurement – this will be with a research assistant who is blind to allocation so instruct participants not to reveal what instructions they were given. Inform research assistant to remind participants not to reveal what instructions they were given. If research assistant not medically trained Karen to perform BP and pulse readings and get participants to sign off on the accuracy.
- At outcomes appointment repeat BP, pulse, safety questionnaire and outcomes questionnaire performed.
- Letter: Participants given letter of thanks with petrol voucher. Letter will also state that they will be informed of the overall trial results when analysed and if they were not in the group with the most effective treatment they will be advised of the instructions for the more effective treatment.

## Appendix AB: Recruitment Procedure

### ARRANGING THE MAIL OUT FROM GENERAL PRACTICE

#### Step one: Generating the patient lists and obtaining practice letterhead

Arrange a time to visit the practice and use a computer that has the querybuild function authorised.

If the practice wants to delegate someone to do this step that is fine – you will need to arrange a time to explain the below process or to email the instructions regarding the querybuild and letterhead.

Request that the computer has excel on it – this will enable you to save directly onto a memory stick. If they don't have excel you will need to print off the entire list per doctor using patient manager (as would be done if an age-sex register query was being printed e.g. for immunisations). If this is the case take along some A4 printer paper with you and advise you will need to have access to a printer to do some printing.

**\*Sign confidentiality agreement before you begin\***

#### In MedTech32:

Tools => Query builder

Name query as Sleep Study x (where 'x' is the name of the general practice)

Select parameters:

"Condition" (select the below one at a time from the left hand column and click the arrow pointing to the right to move these across to become your parameters)

Patient - Dob – Age Between 16 and 75

Patient - Patient (is one)

Patient - funded

Patient - Registered|Equal to Registered

Patient – Provider 'In' *choose doctors names*

In the lower set of boxes repeat the process, moving items across to the lower right hand box

Select

Patient - Provider

Patient - Name Surname

Patient – Name First Name

Patient - Name Preferred

Patient - Address Postal Residence

Patient - Address Postal Street

Patient - Address Postal Suburb

Patient - Address Postal City

Patient - Address Postal Post Code

Click on 'Run Query' box

#### If the computer has Excel:

Once query builder is run, save as an Excel file by saving onto memory stick. If the computer has excel on it, this will automatically save on the memory stick as an excel file. Do not click print! Before you exit check that this has saved correctly by opening the memory stick USB port: my computer=> G: (or whatever the USB port is registering as), there should be an excel file that you can open which has the Dr and patient details on it. Double check that all the fields required have been populated and scan down to the bottom of the list to ensure the approximate expected number are on the list.

#### If the computer does not have Excel:

If the computer does not have excel on it, you will need to click onto record manager (ask the nurse how to do this if you are unsure – it is the same as if an age-sex register query had been run for recalls) and print onto the printer you have been directed to use.

### **Step two: Organising the list for each doctor:**

The Excel spreadsheet needs to be arranged for each doctor.

You need to separate the lists for the doctors. Always keep the raw data saved on 'sheet 1' of the spreadsheet as "raw data". Copy the raw data onto 'sheet 2' of the spreadsheet by selecting all 'Ctrl-A' then copy to 'sheet 2'. Selecting all and then doing a custom sort by column A 'A to Z' will separate out the lists so all the patients for "Dr A" are listed before all the patients for "Dr B". DOUBLE CHECK that the names and addresses match those in the raw data and have been sorted together correctly rather than names and addresses getting mixed up.

Select and 'cut and paste' each doctor's entire list onto a different sheet of the spreadsheet. Once this is done name "Dr A – sorted". Then delete the column A which has the doctor's name (this will be identical for all on the sheet if you have done this correctly). Then select all (Ctrl-A) and sort by doing sort=>custom sort" by column A 'A to Z'. Again, CHECK with the raw data that names and addresses still match up.

You are now ready to print out the patient list for each doctor. Select all and change the font size to 9. In print preview, change layout to portrait. This will show the names and addresses but likely miss of the suburb part of the address – this is ok. Print out the pages that have the names and addresses (you will find a number of pages at the end will only have the suburb/city on them – don't print out these).

Write the doctors name on the top and the total number on the list.

Personalise the 'List cover letter' with name, address, and expected completion date for the doctor and print this out.

### **Step three: Preparing the mail out letter**

You should have an example of their practice letterhead so the mail out letter can be prepared. Print out a personalised copy for the doctor so they can sign this.

Both use the blank 'mail out letter' template. The practice letterhead needs to be inserted at the top (and the word 'letterhead' deleted). There are two ways this can be done:

- 1) Using an electronic example provided by the practice you should be able to copy and paste, resizing as required. Often it will be necessary to make the page margins very narrow so there is room for the larger letterheads.
- 2) Using a paper letterhead provided by the practice can be more difficult. This involves creating an exact replica of the letterhead by matching font and layout. You may want to check if there is a copy that can be emailed to you so you can cut and paste. If you do need to replicate the letterhead yourself, if it is difficult, it is worth checking the practice is happy with the copy you have produced.

When you have a satisfactory letterhead, print off a copy for each doctor, changing the doctors name (and deleting the highlighted "Dr....." on the template first).

### **Step four – having the doctors check their lists and sign a copy of their personalised letter**

Give these 3 items (list, list cover letter, mail out letter) to the doctor in a clear pocket holder. The doctors will cross off any names where they feel it would be unsuitable for their patient to receive a letter or participate in the trial. They will also sign their mail out letter so we can then photocopy this. This also enables them to be aware of the letter that is being sent out from them (they have informed consent by signing this)

Ask your doctors or contact person (practice nurse or practice manager) to let you know when the letter is signed and the list perused. When you pick these up, you will be able to work out how many patients have been crossed off and how many letters are required for the mail out – write these numbers on the top of the patient list.

Arrange for the letter to be photocopied the appropriate number of times (black and white). Enter the data into the 'spreadsheet of practice and doctor info' (thesis>data>patient data).

When you collect the lists vouchers worth \$60 are given in an envelope to each doctor – these must be signed for using the voucher record sheet. If the doctor is not available when you are collecting the list, it is reasonable to be the practice nurse/manager to sign for these. If the practice nurse or manager has been particularly involved/helpful I often give a small box of chocolates (roses or Cadbury favourites).



**Step five: Preparing letters to be posted out**

Using the patient list you have generated above, address the letters and envelopes, insert the correct doctor's mail out letter and the supplied prepaid envelope (with "REFRESH sleep study" stamped on the back or 'REFRESH' handwritten) and post (ensure the letters and envelopes are matching for each doctor!). It pays to only photocopy the letters and print out labels for one doctor at a time so things do not get mixed up.

**If the query was saved in excel you are able to print sticky labels:**

The easiest way to address the envelopes is to use 'mail merge' in Word to print labels selecting data from the patient list in the excel spreadsheet. This can then be printed onto sticky labels which you will be supplied with. Follow the instructions in the Mailings=>Start mail merge expand arrow=>step by step mail merge wizard. Ensure the code of the labels matches that in the mail merge or your labels will be out of synch (e.g. Avery L7157 labels)

**If the query was printed out using report manager:**

You will need to address these by hand.

**Step six:**

If a practice delegate has prepared the list for you then they receive \$40 book vouchers. If they prepare both the list and arrange the mail out they receive \$80 book vouchers. These can be obtained from Karen (they are held by Audrey in the department safe). When these vouchers are delivered they must be signed for on the recording sheet (thesis>chapters>method>trial forms and protocols>protocols). These are then filed in the filing cabinet drawer two.

**Step seven:**

Each time a doctors' mail out has been completed delete their patient list and destroy any hard copy of this by shredding. It is important none of this information is retained. Take care to only save in one or two place so copies are not inadvertently left not deleted. Record where these have been saved. Take care when back up copies of data are made to ensure patient lists are not being duplicated in different places.

## Appendix AC: Processing Postal Responses

### Processing of mail out responses

Mail replies are placed on my desk by Angela when the mail bag is cleared each day  
These are opened.

#### GP letter replies

Those that are replies to the GP letter are divided into two piles:

- 'Insomnia' : these have ticked the following responses:
  - 2a Yes
  - 2b Yes
  - 2c Yes
  - 3  $\geq$ 2 (ie. somewhat/much/very much)
- No insomnia did not tick the above responses.

Those responses with no insomnia are placed in a pile on the lower shelf of the cupboard

#### Printing out Q2

Those with 'Insomnia' are sent sleep disorders questionnaire ('Q2'/ 'Insomnia treatment study') and participant information sheet (PIS) (filed under Thesis>chapters>method>trial forms and protocol>second mail out). The most recent version of the questionnaire is used (look at the date it was last saved).

These are printed out checking that the local printer phprn8 is used (select from drop down menu on print screen that pops up when you press the print button). This prints to the printer at the entrance to the bay that has my desk. Select double sided by selecting the 'properties' box on the print box, then click the Duplex drop down and click 'open to left'. Select the number of copies required on the front screen of the print box.

Print out the questionnaire and PIS, staple them separately. Address a prepaid envelope, fold and insert the questionnaire and PIS and insert a folded freepost envelope (which has been stamped on the back with the REFRESH sleep study stamp). These need to be posted in a standard NZ post mail box (not the yellow mail bag).

The names, GP, contact details are recorded on a spreadsheet 'those who have received second mail out'(This is found under Thesis>data>patient data).

### Processing Q2 responses

#### Check for self harm/thoughts of death

When the sleep disorders questionnaires are received back, it is important to check the answers to the PHQ-9 (Q4b page 4). If anything other than zero is circled for the 'thoughts of death/self harm' question (#9) the GP is contacted as soon as possible and informed of this. If the subject has consented, the questionnaire is then photocopied and sent or delivered to the GP (deliver on the same day if high scores/worrying result). Annotate that the GP has been notified (with date and time) on the front page of the questionnaire.

#### Coding

The sleep disorders questionnaires are coded to check what sleep disorders are present and if the subject has 'Primary Insomnia'. This is done using the sleep disorders diagnosis coding table.

#### Contact primary insomniacs (→refer to Karen)

Those with primary insomnia are contacted to see if they want to participate and to arrange the first meeting to hand out the Actiwatch and sleep diary.

### **No primary insomnia**

If subjects are excluded because of a probable diagnosis of another sleep disorder the reasons are listed on the front page, right hand side under the heading 'exclusions'. On the left hand side the following are noted : 'copy to GP ', 'recorded'  , 'enter ', and 'check diagnoses '.

### **Recording**

Record on the spreadsheet that the reply has been received, if the subject has 'primary insomnia' (coded '1') or not (coded '0') and if not, the alternate diagnoses are recorded. Tick the 'recorded ' box.

### **Photocopy of questionnaire for GP**

Regardless of diagnosis, those who have requested a copy to their GP (bottom of front page of questionnaire) have their questionnaire photocopied and posted or delivered to their GP. The 'copy to GP' box is then ticked. The originals are filed in the 'to enter' box in the top drawer of the filing cabinet.

Generally, a pile of responses from the same GP will arrive in closed succession. Generally, the photocopies for the same GP are bundled together every 2 weeks or so and posted/delivered.

Those who would not like their GP to have a copy have only 'enter ', and 'check diagnoses  ' written on the left hand side of the front page of the questionnaire. These are then placed directly in the 'To enter' box in the top drawer of the filing cabinet.

**Entering data** (currently not being done – not essential to trial, but intention is to do this later as time permits)

The data from the pile of Q2 responses (those who have not made it onto the trial) is to be entered as this will give a good overview as to what sort of sleep problems are in the general practice community. By doing this process, the original coding of the Q2's is checked, so the boxes for 'check diagnosis' and 'enter' can both then be ticked.

The responses are then stored in an 'Entered' box – also held in the top drawer of the filing cabinet.

# **Patients with INSOMNIA?**

Hello! My name is Karen Falloon and I am a part-time GP (FRNZCGP) and PhD candidate. For my doctoral research I am running a trial looking at behavioural treatments for primary insomnia through the Department of General Practice with Professor Bruce Arroll and Dr Tony Fernando (psychiatrist and insomnia specialist).

**I am testing a new non-pharmacological brief intervention (bedtime reorganisation regime) for primary insomnia so GPs will have more effective options for treating insomnia.**

To find those with primary insomnia I am recruiting through general practices in the Auckland area. If you have any patients with insomnia who may be interested in the study – please refer them to us

NB: Those on long-term, nightly hypnotics are advised to undertake a managed withdrawal from their medication prior to participation. Those using occasional/intermittent sleeping pills are considered.

**We are looking for patients with primary insomnia for our study into a behavioural treatment for insomnia\***

Your patients can be advised to contact us at [sleepstudy@auckland.ac.nz](mailto:sleepstudy@auckland.ac.nz)  
or phone 373 7599 x

\*(Excluded from the study are patients who have been diagnosed with a specific sleep disorder such as OSA or restless leg syndrome)

**Please circulate this fax to the doctors and nurses in your practice.**

# INSOMNIA

Can't get to sleep?

Can't stay asleep?

Waking too early?

⇒ Is this affecting your life?

⇒ Does this occur despite giving yourself enough opportunity to sleep?

⇒ Are you otherwise well & aged between 16 and 75 years old?

*If yes...*

You may be suitable for our study of a non-drug technique to improve sleep

Email: [sleepstudy@auckland.ac.nz](mailto:sleepstudy@auckland.ac.nz)

Or ask reception for a self-referral form

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